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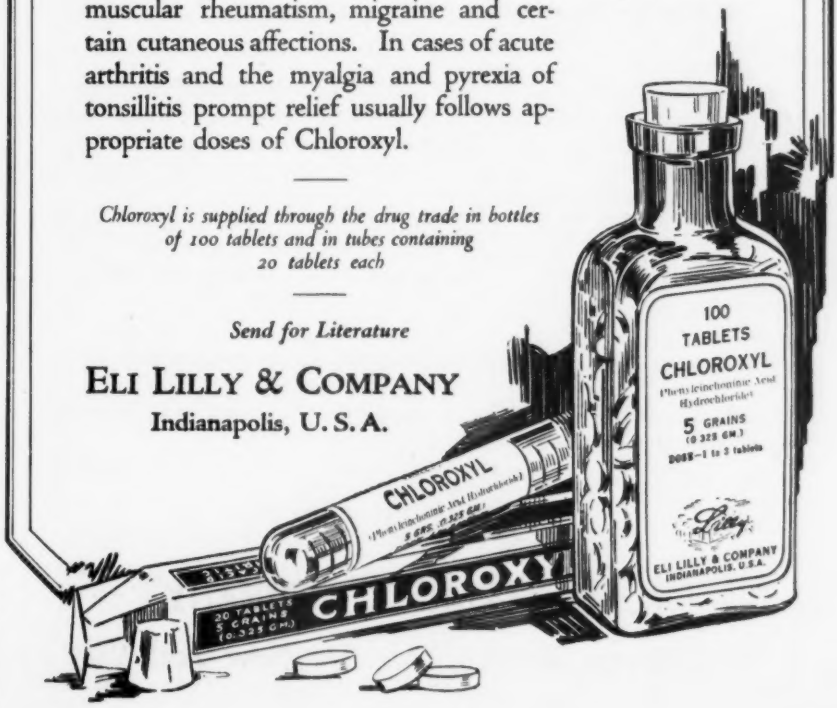

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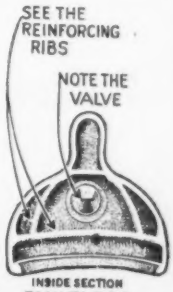

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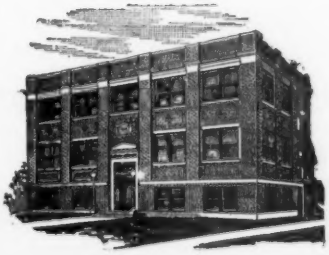

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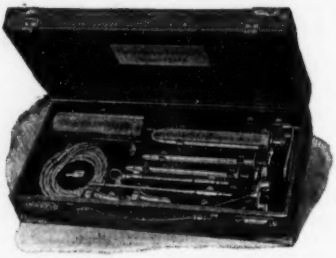

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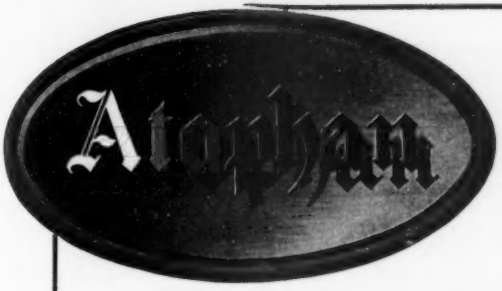

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AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

APRIL, 1920

ORIGINAL ARTICLES

CARCINOMA OF THE DUODENUM.

By J. B. Deaver, M.D.,

AND

I. S. Ravdin, M.D.,

PHILADELPHIA.

Carcinoma of the duodenum is of sufficiently rare occurrence to warrant the recording of cases.

The patient whose history follows was admitted to the University Hospital June 12, 1919:

M. O., aged sixty-three years; white; male.

Chief Complaint. Pain in the right side of the abdomen.

History of Present Illness. About five months ago he first noticed pain in the right upper abdomen, coming on just after meals, and usually worse at night. He was nauseated at such times and belched gas very freely and frequently, but never vomited and has never been jaundiced. For over a year he has been distended after meals and has belched gas quite freely, with relief; he had no actual pain until five months ago. Since onset he has lost thirty-four pounds. Pain has been practically constant ever since onset, recently radiating to the back, and becoming steadily more and more severe. Eating seems to relieve the pain for a short time. No genito-urinary symptoms.

Previous medical history, social history and family history negative.

Physical Examination. Adult male, apparently about seventy years of age, poorly nourished and underdeveloped. He complains at intervals of severe pain in the right hypochondrium, radiating to the back, but at other times is apparently quite comfortable. Skin is rather swarthy; no jaundice; no cyanosis; no eruptions.

Blood-pressure. 143 to 47.

Head. Well-formed, with no gross abnormalities. Temporals are fairly hard but not nodular or tortuous.

Eyes. No congestion. Pupils well contracted, responding promptly to light and in accommodation, equal and regular; no nystagmus; no extraocular palsies. Both lenses are apparently partly opaque, and the left one shows a distinct black streak on examination by the ophthalmoscope. Eye-grounds are dimly seen but appear to be of good color, with prominent and glistening arteries; no hemorrhages; no exudates.

Nose. Moderate deflection of the septum to the right; no obstruction.

Ears. Negative.

Mouth. Lips moist and of good color. Teeth in very bad condition. Many are gone, and those remaining are discolored and show plenty of pyorrhea. Tongue is broad and moist, with a heavy white coat; protrudes normally. Pharynx is moderately congested, with a thick coating of mucus. Tonsils are not visible.

Neck. No adenopathy; no abnormal pulsations; no tracheal tug; no thyroid enlargement.

Chest. Rather poorly formed, with fair expansion, equal and regular throughout. Resonance, fremitus and voice and breath sounds are physiological. No rales or frictions.

Heart. R. B., 2.5 cm.; R. O., 9; L. B., 10.5 cm.; L. O., 13 cm.; height, 7 cm. Apex-beat not visible or palpable. Sounds very distant and of poor muscular tone; no undue accentuation; no murmurs. There is an occasional tendency to bigeminate rhythm, with the second of the sounds louder than the first, probably ventricular extrasystoles. No other arrhythmia.

Abdomen. Scaphoid. Distinct cardiac pulsation in the epigastrium. Left side is not tender or rigid and the spleen is not palpable. Right rectus is rigid throughout, more so in upper third, which is also very tender to palpation. There is fulness in the epigastrium that suggests a firm, fixed mass below. Liver is not palpable. Left inguinal canal is weak at lower third and gives impulse on coughing, and when not restrained a hernia protrudes there. Left external ring also patulous and gives impulse on coughing. Right side apparently normal. No adenopathy.

Extremities. Poorly muscled. No paralysis; no sensory abnormality. Reflexes normally present throughout. No Kernig; no Babinski; no clonus. Moderate radial sclerosis. No tortuosity. No nodules.

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July 21. Urine: Light amber; cloudy; flocculent sediment; specific gravity, 1.026; acid reaction; albumin, 0; sugar, 0.

Microscope shows: Casts, 0; cylindroids, 0; mucus, +++; red blood cells, 0; white blood cells, 1 to 2; epithelium, +; crystals, 0.

Blood Wassermann, negative.

July 25. *Gastric Contents.* Quantity, 100 c.c.; normal odor; white color; total acidity, 94; free HCl, 64; occult blood, 0. Starch, +++; yeast, +; fat, ++; other food masses, 0; occasional epithelium; mucus, +; Oppler-Boas and sarcinæ, 0.

Gastro-intestinal Roentgen-ray Report. Stomach: Adhesions or possible ulcer near pylorus. Duodenum: Probably negative. Colon: Fair position. Marked stasis. Exquisite tenderness always over right iliac fossa region, cause not determined.

July 26. Phenolphthalein elimination—intravenous: First hour, 50 per cent.; second hour, 10 per cent.; total, two hours, 60 per cent.

Blood-urea nitrogen, 18 mg. per 100 c.c.

Blood: Red blood cells, 4,700,000; white blood cells, 9800; hemoglobin, 70 per cent.

Differential: Neutrophiles, 68 per cent.; lymphocytes, 24 per cent.; large mononuclears, 4 per cent.; transitionals, 4 per cent.; eosinophiles, 0 per cent.; basophiles, 1 per cent.

Tentative Diagnosis: Carcinoma ventriculi.

August 11. Operation: Right rectus incision; stomach enlarged and somewhat ptosed. There was a sheet of "pathological peritoneum" stretching across the duodenum to the edge of the liver, which was seen by the roentgen rays, obstructing a view of the gall-bladder. The first part of the duodenum was markedly dilated. The "pathological peritoneum" was separated and the gall-bladder was found to be apparently normal except for a slight dilatation. The marked dilatation of the duodenum was the outstanding feature. Palpation of the duodenum disclosed a hard, irregular mass on its inner posterior wall near the termination of the second portion. The duodenum was mobilized. It was then opened and the ulcerated carcinomatous mass was found to originate below the papilla of Vater. It had invaded the head of the pancreas to such an extent as to make the point of differentiation impossible. A section was taken out for diagnostic purposes and the duodenum closed. A posterior gastro-enterostomy was then performed and the abdomen closed without drainage.

August 11. The patient reacted well from the operation.

August 12. Feels well. Some pain. Peristalsis started. Given albumen.

August 13. At 6.40 A.M. patient suddenly had leaky skin. Shock. Pulse absent at wrist. Heart dilated both ways. Skin pale and leaky. Given atropin because of beginning pulmonary edema. Given digalin and camphorated oil, minims xv each. Condition unimproved and patient died of cardiac failure at 8.40 A.M.

Pathological Report. Dr. Weidman. Duodenal carcinoma. Frozen section shows complete loss of surface epithelium, the base consisting of a mass of nondescript material which gives way more deeply to a more or less devitalized fibrous tissue heavily infiltrated with lymphocytes and plasma cells. Still deeper the fibrous tissue becomes looser, more cellular, and in the very deepest parts of this fibrous layer shows acini of a cancerous type—that is, they are irregular in distribution and shape and have a rather active proliferating type of epithelium. In one or two instances such acini abut directly upon the muscular tunic, and selected places can be seen extending between the bands into comparatively deep positions. The invasion in the section

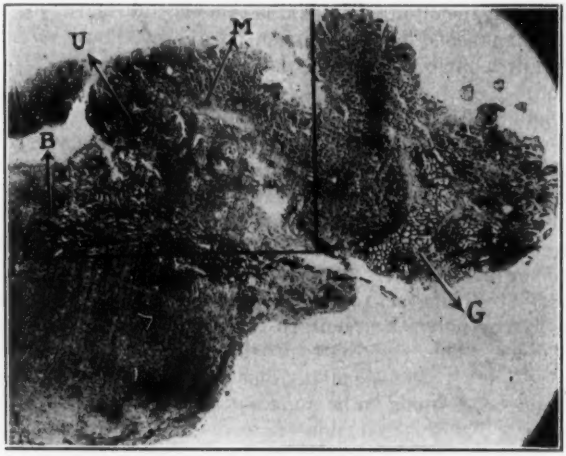

FIG. 1.—Low-power view of margin of ulcerated area. The more normal duodenal mucosa at extreme right, showing Brunner's glands at *G* and muscularis mucosa at *M*. Margin of ulcer at *U*, where the carcinomatous change is developed. Base at *B*. The upper left-hand rectangle is shown in higher magnification in Fig. 2.

studied cannot be definitely traced from the surface epithelium, and the type of acinus leads one to the opinion that it does not extend from such, but rather from a more alveolar type of glands, such as the pancreas or Brunner's glands. The muscle fibers in the external coats show granular cytoplasm and some shrinkage of nuclei, indicating a devitalized condition well short of necrosis.

Additional sections prepared by the paraffin method show an undoubted carcinoma of adeno type. Furthermore, it is perfectly clear that the tumor has sprung from the surface of the duodenum and not from Brunner's glands or the pancreas.

Postmortem Examination. A complete postmortem was not

obtainable, so an inspection was made through the original operative incision. The operative site was in excellent condition.

At the terminal end of the second portion of the duodenum was a grayish, ulcerated, indurated mass, approximately 2.5 cm. square, which was continuous with two distinct indurated masses about 2 cm. in diameter in the head of the pancreas.

There was no obstruction of the common bile duct, nor evidence of obstruction of the pancreatic ducts, nor other evidence of metastasis.

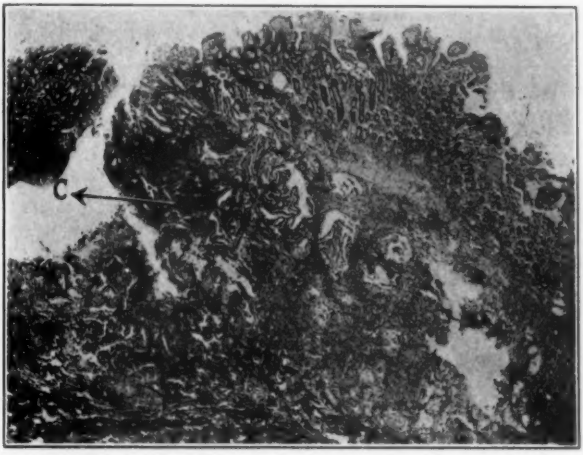

FIG. 2. — High-power view of Fig. 1. Transition from the more normal to the neoplastic is occurring in the darkly stained region at *C*. Compare with Fig. 1.

Notes on the Clinical Aspect of the Case. It is probable that this case is one of primary duodenal carcinoma, although the history is very similar to that of ulcer. The rapid loss of weight and the rather short duration of the disease, on the other hand, would point to primary carcinoma. It is remarkable that with such extensive involvement the patient should not have had any vomiting.

The duration of life in primary duodenal carcinoma varies according to various writers Fenwick gives seven months as an average while Pic gives from three months to a year.

Frequency of Carcinoma of the Duodenum. Primary carcinoma of the duodenum is a very rare disease. According to the reports of the Mayo Clinic only 3 per cent. of carcinomas of the entire intestinal tract originate in the small intestine. Of 3563 cases of malignant tumors of the intestine, Brill found only 2.5 per cent. in the small intestine, while Jefferson in 4177 collected cases of intestinal carcinoma finds 3.1 per cent. to be duodenal.

The following tables will give an idea of the relative frequency

of duodenal carcinoma and its relation to carcinoma in other parts of the small intestine:

TABLE I.

Author.	Source.	Total autopsies.	Duodenal carcinoma.
Schleringer	Vienna	42,000	7
Nothnagel	Pathologic Institute, Vienna	21,358	5
McGlinn	Philadelphia General Hospital	9,000	1
Rüpp	Zürich	4,258	1
Fr. Müller	Basle, 1874–1904	11,314	6
Fenwick	London Hospital	19,518	18
M. Müller	Berne, 1886–1891	5,621	6
Perry and Shaw	Guy's Hospital	17,652	4
Maydl	Wiener Allgemeines Krankenhaus	20,480	2
		151,201	50

Average incidence of carcinoma of the duodenum, 0.033 per cent.

TABLE II.

Author.	Duodenal carcinoma.	Jejuno-ileal carcinoma.
Köhler	9	3
Mayo	5	17
Nothnagel	7	11
M. Müller	6	3
Rüpp	1	1
Barnard	5	10
Lubarsch	2	2
Fr. Müller	6	2
Maydl	2	4
Schlieps	20	16
	63	69

Average of duodenal carcinomas, 47.7 per cent.

Average of jejuno-ileo carcinomas, 52.2 per cent.

Of 343 cases of intestinal carcinoma collected by Nothnagel at the Pathological Institute between 1870 and 1893, 7 were in the duodenum and 11 in the ileum; and of 542 cases collected by Schlieps, 20 were in the duodenum and 16 in the ileum; while the Mayo Clinic, in 1846 cases of carcinoma of the intestine, finds the duodenum involved in 5 cases and the ileum 6, and the jejunum 11 times.

Situation and Relative Frequency at Various Sites of Duodenal Carcinoma. Pic's topographical classification is as follows:

1. Parapyloric.
2. Peri-ampullary.
3. Perijejunal.

Ewing classifies them as:

1. Carcinoma following ulcer.
2. Carcinoma at the papilla of Vater.
3. Carcinoma of the third portion of the duodenum.

While the Mayo Clinic classifies them as:

1. Supra-ampullary.
2. Ampullary.
3. Infra-ampullary.

TABLE III.

Author.	First part duodenal.	Second part.	Third part.
Mayo	5[1]		
Rolleston	8	24	3
Geiser	11	51	9
Fenwick	11	29	7
	35	104	19
Percentage	22.15	65.82	12.02

These statistics seem to show that taking the small intestine into account, inch for inch, the first portion of the duodenum is more likely to undergo malignant degeneration than other portions of the small intestine, and in the duodenum *per se* we find that the second portion is much more liable to undergo malignant change than is the first or third portion. This is undoubtedly due to the presence of the ampulla of Vater and the occasional separate opening of the pancreatic ducts. The incidence of carcinoma of the first portion of the duodenum, on the other hand, may be due to the fact that this is the favorite site of duodenal ulcer. How frequently carcinoma of the duodenum is engrafted upon a chronic duodenal ulcer is, of course, uncertain. One thing is certain, that carcinomatous degeneration is not nearly so frequent in duodenal as in gastric ulcer.

Letulle, Perry and Shaw and Nathan-Larrier have reported 10 cases while Jefferson has collected 20 more, making a total of 30 cases in the literature in which evidence was found that duodenal ulcers had undergone malignant change. The location of these tumors chiefly near the pylorus agrees with the statistics as to the site of chronic duodenal ulcers; Collins in 262 cases reports 242 cases of involvement of the first portion and 14 of the second.

Pathology. 1. Carcinoma following duodenal ulcer differs little from that of pyloric ulcerocarcinoma. The lumen of the duodenum is nearly always encroached upon. There is a tendency to early metastasis. The stomach is frequently greatly dilated. It is likely that many of the so-called pyloric carcinomas which are operated upon, probably arise from the duodenum and extend into the pylorus.

2. Carcinoma of the second portion most frequently arises in or about the papilla of Vater. Jaundice is a very constant and persistent symptom, although it is not so severe as in carcinoma of the ampulla. There is frequently a dilatation of the biliary and pancreatic ducts, with the formation of pancreatic retention cysts. Krause, Jefferson, Gerster and Geiser have also observed fat necrosis in these cases. The structure is commonly that of a cylindrical-celled adenocarcinoma. Frequently the tumors, as in

[1] Several of these cases also involved the papilla of Vater.

the case described, are very closely associated with a mass in the pancreas, while occasionally microscopically a duodenal carcinoma resembles pancreatic tissue and not the cells of the cylindrical variety, so that an origin from pancreatic rests has been suggested. Branham has reported one such case. Others have noted the presence of Brunner's glands in these growths. A case of this type has been reported by Orth.

3. Carcinoma of the third portion, as our Table III shows, is the most infrequent of all carcinomas of the small intestine. Most of these take the form of a broad, flat, ulcerating mass, with stenosis. There is dilatation of the first and second portion of the duodenum. The structure is usually a cylindrical-celled or an alveolar carcinoma.

Diagnosis. If a tumor is palpable it is not easy to distinguish it from a tumor of the pylorus. Tumors of the second or third portion are usually fixed while those of the pylorus or first portion of the duodenum are movable.

Pyloric tumors are usually associated with more marked symptoms of gastric obstruction and dilatation, except in the high cases of the first portion of the duodenum. Jaundice points to carcinoma of the duodenum, as does a normal acidity of the gastric contents, while in carcinoma of the stomach dyspeptic symptoms occur earlier and are more serious.

Tumors of the second portion, especially the papillary ones, may prove fatal by biliary obstruction and severe infection. These cases may terminate by sudden single or repeated hemorrhages.

In cases associated with obstruction of the pancreatic ducts, Einhorn called attention to pancreatic diarrhea, the patient having copious, fatty, pale and offensive stools containing recognizable portions of undigested food.

In tumors of the third portion gastric symptoms with vomiting of great quantities of biliary material are prominent.

SUMMARY. 1. Carcinoma of the duodenum is a rare condition. It is found in 0.033 per cent. of hospital autopsies.

2. The percentage of carcinomas of the entire intestinal tract orginating in the small intestine varies from 2.5 per cent. to 3.1 per cent.

3. The relative proportion between carcinoma of the duodenum to that of the jejunum and ileum is 47.7 per cent. to 52.2 per cent.

4. Inch for inch the duodenum is much more liable to undergo carcinomatous change than the jejunum or ileum.

5. The relative frequency at various sites of duodenal carcinoma is as follows: First portion, 22.15 per cent.; second portion, 65.82 per cent.; third portion, 12.02 per cent.

6. Carcinomatous degeneration of chronic duodenal ulcers is not nearly so frequent as in chronic gastric ulcers.

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NUTRITION AND PUBLIC HEALTH WITH SPECIAL REFERENCE TO VITAMINES.[1]

By J. F. McClendon, Ph.D.,

ASSOCIATE PROFESSOR OF PHYSIOLOGY, UNIVERSITY OF MINNESOTA MEDICAL SCHOOL, MINNEAPOLIS, MINNESOTA.

Notwithstanding the fact that my first biological interest was in relation to the subject of nutrition, my earlier experiments were made on myself and were discontinued as soon as my curiosity was satisfied, and I have had occasion to work out, in a scientific manner, only small details of this vast subject. While serving with the Division of Food and Nutrition, Medical Department, U. S. Army, I was impressed with the wide differences of opinion that exist in

[1] Published with permission of the Surgeon-General, U. S. Army.

the public mind, and especially among the medical profession, on this subject, and since January 1, 1919, with the assistance of ten students, I have devoted nearly all of my time to investigation in this field, the results of which are being published in the *Journal of Biological Chemistry*. Owing to the fact that the changed economic conditions due to the war have brought about some changes in dietary habits, the effects of which may not be thoroughly appreciated until some years have passed, a compilation of some of the literature and discussion of some of the problems may not be out of place at this time. Since vitamine studies are receiving considerable attention just now, attention will be directed especially to them throughout most of this paper. Other subjects will be treated more briefly, not because they are less important, but because they are better understood.

Effect of Fuel Value of Diet on Body Weight. Benedict, Miles, Roth and Smith have so thoroughly investigated the effects of a restricted diet (about 2 ounces protein and 2000 calories per ration) that further comment seems unnecessary. Similar restrictions of diet have been voluntarily or involuntarily made by large numbers of persons during the war. One common conclusion from these experiments may be emphasized here, since I have heard it repeatedly denied by persons who had no reliable information on the subject, and that is that the body weight is just as much dependent on the calorific value of the food in man as in animals. Perhaps many persons partake of a low calorific diet in the presence of an abundance of food, owing to various factors that reduce the appetite. In animal experiments a diet that is inadequate in regard to some constituent reduces the appetite. This has been especially noticed in experiments in which one or more of the amino-acids or vitamines was deficient in quantity. Animals on a vitamine-free diet finally refuse food entirely. This factor may be suggested as a possible danger in so-called low protein diets.

As early as 1887, Hirschfeld advocated a low-protein diet and the same ideas have been proposed by many scientific and unscientific propagandists since that date. In 1898, while a university student, subject to compulsory physical exercise, I restricted my diet for three months in regard to the quantity of animal foods taken. My weight dropped to 70 pounds and my skin became rough, the hair on my body and face standing at right angles to the skin surface. At the end of this experiment I partook of a liberal diet, including fresh meat and vegetables, eggs, milk, beef fat, cod-liver oil, raw bone-marrow and malt extract, and at the end of one year my weight was 140 pounds, showing a gain of 3 ounces per day. In order to distinguish between quality and quantity of the diet I made another experiment in 1912. After having maintained a fairly constant weight under certain conditions for several years, and without consciously disturbing those conditions, I added about

2 ounces of cottonseed oil per day to my diet and gained 3 ounces per day for eighty days. Since the oil was drunk after meals it did not interfere directly with my appetite, and since it is not known to contain a vitamine or other growth-producing substance, it probably acted purely through its calorific value or was stored, together with water, as adipose tissue. Since fat does not cause excessive water storage, as is the case with carbohydrate, the increase of about 15 pounds in weight cannot be attributed to water storage alone.

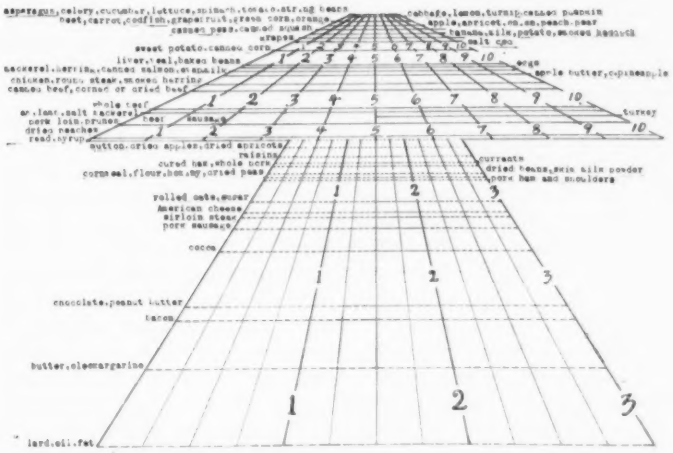

Chart for rapid calculation of fuel value of diet. The calorific value of any food may be calculated from its weight in pounds by finding the name of the food in the chart and the number corresponding to its weight on the line containing its name. Apply a millimeter tape to the scale on the chart and each millimeter represents 100 calories. In the upper part of the chart the scale reads in pounds from one to ten. In the lower part of the chart the scale reads in pounds from one to three and further divisions signify halves and quarters of a pound and the breaks in the horizontal lines signify ounces. Foods of the same calorific value are on the same line and their weights may be added together before using the chart. In order to use the chart for simultaneous multiplication and addition, prepare the list of foods in pounds and measure the pound scale of each successively with the millimeter tape, commencing each measurement on the tape at the end of the preceding one. The final figure on the tape with two ciphers added represents the total number of calories of the entire list of foods.

Although a restricted diet has been advocated by Horace Fletcher, Chittenden, and more recently by Hindhede, these propagandists seem to be in the minority. Another point of view is illustrated by the excuse a slave gave for stealing a chicken: "Nigger meat's wurf mor'n chicken meat." There are some uses of a restricted diet, however, but the difficulty lies in enforcing the dietary rules. It is said that in the treatment of obesity at Carlsbad the patients were served very small portions at high prices *à la carte*.

In economical rationing a rapid and inexpensive method of calculation of fuel value of food is desirable. By means of the chart shown, simultaneous multiplication and addition is performed in calculation of the calorific value of a list of foods. The time required is chiefly used in finding the name of the food on the chart, and hence speed increases with practice. The first time I used this chart the percentage error and the number of minutes required were carefully noted. The food used by the 9th Engineers in one week was used in the test. It required five minutes to calculate the calorific value of this food with the chart, and the error was 5 per cent. By taking more time to read the chart, or by using a chart on a larger scale, greater accuracy may be obtained in the calculation, but since the accuracy of the data may not exceed 5 per cent., greater accuracy in calculation may not be desired.

Reaction and Bacteriology of the Alimentary Tract. The reaction of the alimentary tract is important in relation to the character of the hydrolysis of the food, either due to digestive juices or bacteria. The saliva in the closed mouth is about neutral. The gastric juice is about one-tenth normal hydrochloric acid and the exact hydrogen ion concentration of the stomach contents depends on that of the food and the relative quantity of gastric juice that has been secreted (as well as the degree of mixing.) McClendon and Sharp have shown that with the occasional exception of fresh milk, both raw and cooked foods are slightly acid. It should be noted that in the paper by McClendon and Sharp the first table (quoted from Clark and Lubs) should be omitted, since acid or alkali had been added to the food juices in many cases. The low acidity of the contents of the infant's stomach after feeding is not so much due to lower acidity of the gastric juice as to the diet of fresh milk, and possibly to the small quantity of gastric juice secreted. It was shown by McClendon, Myers, Culligan and Gydesen that the small intestine is slightly acid in young and adult carnivora and young herbivora. In adult herbivora, however, the duodenum is usually slightly acid, but this passes over to a slightly alkaline reaction somewhere in the small intestine. The reaction of the rabbit's intestine could be changed from alkaline to acid by flooding it with soluble carbohydrate, as by adding lactose to the diet or feeding carrots exclusively.

According to Metchnikoff the presence of acid-producing bacteria in the intestine inhibits the growth of putrefactive forms. Torrey has shown that flooding the intestine with soluble carbohydrate, especially lactose, increases the ratio of the acid-producing to the putrefactive bacteria. This is in line with the fact that the ingestion of soluble carbohydrate changes the reaction of the rabbit's intestine from alkaline to acid. Perhaps it is the acid reaction of the intestinal contents that inhibits the growth of putrefactive bacteria. Exercise, by causing more rapid absorption

of water from the intestine, may decrease the growth of bacteria, whereas in diarrhea the increased fluidity increases bacterial growth.

Besides the common bacteria of the intestine just mentioned, that are always present, and whose relative numbers depend on the soluble carbohydrates present, other bacteria that are normally absent appear as infections, as, for example, the typhoid and paratyphoid group. It seems possible, also, that other less virulent, unidentified bacteria may play a part in altering the normal conditions of nutrition.

COOKING. In *The Complete Cook*, 1805, which is the revised and corrected edition of *The Frugal Housewife*, the following sentence may be found in the preface: "The chief excellence of all cookery consists in a perfect acquaintance with the making of gravies and sauces." That is not the aspect of cooking to which reference will be made. The natural flavors of foods with the addition of salt, which is a necessary ingredient of the diet, should be sufficiently attractive to the hungry man. The necessity of cooking lies in two circumstances: (1) it is necessary to gelatinize the starch in starchy foods in order to make it utilizable and (2) it is desirable to kill certain pathogenic organisms or destroy bacterial toxins when present. Most starches gelatinize in water of 70° C. in a few moments, and prolonged cooking is only necessary in case the food is so dry that prolonged soaking is necessary to wet it (and the heat merely shortens the time necessary to soak it). Cooking softens food so that it is easier to chew, but that may not be wholly desirable. If it is desired to gelatinize collagen a high temperature or prolonged duration is necessary, but gelatin is too deficient a protein to be much sought after.

Many persons who would not eat a rare steak see no necessity in cooking canned goods. From the standpoint of danger from bacterial agencies, however, it is more necessary to sterilize preserved foods than fresh ones. Many cases of botulism are due to eating canned foods or tasting them to see whether they are spoiled, and it is stated that cooking destroyes the toxin of Bacillus botulinus. Since cooking reduces the vitamine content of foods any unnecessary cooking is to be discouraged. Fresh foods if kept clean should be eaten raw or rare, whereas preserved foods, as a rule, should be cooked. Pork and fish should be sterilized because they are liable to contain parasites that escape detection. Mixtures of meat and vegetables should not be allowed to remain long uncooked, because numerous spore-bearing bacilli on the vegetables multiply rapidly in the meat juices.

Many persons object to visible fat in cooked food; in fact, some cooks remove fat from the surface of soup with blotting paper. Fried foods are said to upset delicate stomachs, and this has been attributed to the action of heat in setting free fatty acids. It has been shown, however, by the War Committee of the Royal Society

that free fatty acids in relatively large quantities may be eaten without disagreeable effects. Perhaps the irritant action of some fried foods may be due to the formation of acrolein. Since this occurs only in case the temperature is raised to 300° C., there is no necessity for it. The fat of all foods should be eaten as an economical measure.

Food Preservation. The most ancient and widely used method of food preservation is by desiccation. The seeds of plants are usually desiccated before they are gathered for food. The desiccation of root vegetables was practised by various savage tribes and the drying of meat and fish was perhaps as common a practice. Hawk calls attention to the fact that dehydrated vegetables when soaked up again hold their water much less tenaciously than fresh vegetables do. This has been known as a characteristic difference between live and dead tissue, and the living state is associated with electrical polarization of the cell surfaces, which would partially explain the holding of water. In fact, it is the tenacity with which foods hold to water that adds largely to the cost of dried foods. In the drying of prunes, decomposition usually takes place unless the prunes are first dipped in an alkaline solution, so as to make them permeable to water. In the desiccation of tissue for biochemical analyses it has long been known that decomposition of phosphatides and oxidation of unsaturated fatty acids occurs if the moist or dried tissue is exposed to air, and similar decomposition must occur in dried foods.

Various forms of pickling and preserving in which the addition of salt or sugar occurs is similar to drying, in that the antiseptic action of salt and sugar is partially due to their dehydrating effect on bacteria. The use of other antiseptics is so limited as to be of minor importance.

The process of canning might be considered next to refrigeration in excellence as a method of preserving food, but unfortunately, complete sterilization and exclusion of air does not always occur. In the canning of milk, partial desiccation is also performed.

In the process of cold storage, vegetables and fruits remain alive, and it is claimed that fish may be kept alive in cold storage by the Pictet process. The growth of penicillium on beef in cold storage hastens ripening and the beef does not become toxic until the taste changes to musty or bitter. Beef is the best meat for cold storage on account of its large size and low water content and mechanical density, which inhibit the penetration of microörganisms. Cold storage is the only method of food preservation that maintains the total vitamine content.

Proteins, Fats, Carbohydrates, Salts and Water. The protein factor in nutrition has been so exhaustively treated by Osborne and Mendel and others that it cannot be reviewed here. A a general rule animal proteins are more complete in amino-acid

content than are those of vegetable origin. According to Goldberger, Wheeler and Sydenstriker, families in which pellagra occurred consumed 3 ounces of protein per man per day, but only 25 per cent. of it was animal protein. Since a nitrogen balance may be maintained in skinny individuals on less than 3 ounces of protein per day, we may assume that 3 ounces is sufficient, provided it is all animal protein; but that in case of mixed proteins, and in the absence of more definite knowledge, it is not wise to make a special effort to limit the protein intake. Under modern conditions there seems to be no defence for vegetarianism. Clark finds a high protein diet increases the rate of healing of wounds. It is also useful in case of profuse pus formation to replace the lost protein.

In addition to the fact that some fats contain vitamines, fats are necessary in the diet to decrease its bulk. In a diet of 3000 calories it would require 10 pounds of potatoes or other vegetables or fruits for the three meals, and if we include the saliva and other fluid swallowed and the gastric juice secreted the stomach would receive a load of about 8 pounds per meal (not all at once, however). Hardtack would be less bulky, but would increase salivation and thirst. The Interallied Scientific Food Commission fixed the minimum fat ration at 75 grams.

So far as investigations have progressed, muscular work depends on a supply of carbohydrate (compare Anderson and Lusk). In the absence of carbohydrate, fat is incompletely oxidized (for heat production) and yields products that may be toxic. Both man and the dog may live for considerable periods without carbohydrate in the food and probably depend for muscular energy on the carbohydrate radicle of phosphatides and glycoproteins and especially on the synthesis of glucose from glycerin and deaminized amino-acids; but there seems to be no advantage in such a diet. The flooding of the intestine with soluble carbohydrate retards putrefaction of proteins.

Salts are necessary, but since all factors causing their excretion have not been thoroughly investigated the minimum requirement is uncertain. Sodium chloride should be added to food, but it seems probable that the other salts are present in a mixed diet in sufficient quantity. Since milk and fresh vegetables that are rich in salts are also rich in vitamines that cause relative retention of salts, all that can be said is that milk and fresh vegetables are advantageous, and we are not justified in substituting an inorganic salt mixture for them. No harm can arise, however, in the addition of such a mixture to an apparently adequate diet.

The necessity of water in the diet needs no comment, and Hawk and his collaborators have shown that no ill-effects follow water-drinking at meals. The salt content of drinking water is usually insignificant, and the arguments for lithia water have been shown to be fallacious.

VITAMINES. Owing to the fact that differences of opinion exist among investigators as to the number of vitamines, the classification made by the British Committee on Accessory Food Factors will be followed. Hopkins studied "Accessory factors in food." Funk called these vitamines, and McCollum and Kennedy claim there are only two vitamines, which they call fat-soluble-A and water-soluble-B. Drummond refers to the antiscorbutic factor as water-soluble-C. McCollum and Kennedy's A-factor is also called fat-soluble or antirachitic vitamine, and their B-factor is called antineuritic vitamine, whereas Drummond's C-factor is usually called antiscorbutic vitamine.

The fat-soluble or antirachitic vitamine is very abundant in yellow fats of animal origin. It is deficient in pig fat because the pig eats few leaves, and in hydrogenated or hardened fats and free fatty acids because it is destroyed by the heat and chemical agents used in manufacture. It is deficient in vegetable fats except perhaps in peanut oil. It is synthesized in green leaves, and carnivorous animals depend for their supply on the bodies of grazing animals in which it has been extracted from the green leaves eaten and stored in the body fats. It is abundant in the germ of seeds, especially yellow seeds but deficient in degerminated cereals. It is present in potatoes, carrots and bananas, being most abundant in the yellow colored roots (carrots and sweet potatoes). According to McCollum the milk of cows is richer in fat-soluble-A when more is present in the cow's food. According to Osborne and Mendel, 1916, this vitamine is not destroyed in butter fat by storage for a year. According to Drummond, fat-soluble-A is not carotin.

The antineuritic vitamine seems to be most concentrated in the seeds of plants and eggs of animals. In cereals it is present in the germ but absent in the endosperm and bran (unless the bran contains the germ. It is abundant in yeast and in animal gland tissue, but muscle tissue and milk do not contain an oversupply. Both leaf and root vegetables and fruits contain it in small amounts. Cooking reduces the quantity of this vitamine. As first observed by Frazier and Stanton the content of food products from the same source in this vitamine runs parallel to the phosphorus content. According to Voegtlin and Myers, both antineuritic and fat-soluble vitamines of wheat and corn products run parallel to the phosphorus content.

The antiscorbutic vitamine seems to be present in all living tissue and fresh food, and is especially abundant in acid fruits, tomatoes, cabbage and turnips. It is more or less abundant in all fresh, raw vegetables. It is very sensitive to alkali, heat, desiccation and storage at ordinary temperatures, and hence is deficient in cereals and dried or canned meat and vegetables, except canned tomatoes. The acid in tomatoes and fruits seems to protect it during the heating and it is useful to class tomatoes with fruits, as

is done by British writers. It is present in milk in small amounts. Dutcher has shown that young guinea-pigs grow better and are healthier on milk from a cow on green feed than of a cow on dry feed. Scurvy developed very quickly on winter milk, but did not develop (in the same length of time) on summer milk. The milk was skimmed in both cases to prevent diarrhea. This indicates that the antiscorbutic vitamine in milk depends on that in the cows' feed, and may explain why some breast-fed babies have scurvy if the food of the mother is deficient in antiscorbutics.

VITAMINE REQUIREMENTS AND DEFICIENCY DISEASES. Since the composition of vitamines is unknown and their distribution among foodstuffs is known only in a general way, it is not yet possible to work out the vitamine requirements with even as much certainty as has been done in the case of food constituents of known composition. Experiments on animals and observations on man indicate that vitamine deficiency manifests itself more slowly the longer the average life (in different species) and the more mature the individual (in the same species). It is also necessary to know that the individual has been getting an adequate supply of vitamines before the beginning of the experiment in order to determine the duration of vitamine deficiency that it can stand. Even with this precaution, variations in results may be obtained owing to lack of knowledge of the degree of vitamine deficiency in the food. At present the vitamine content of foods can only be determined by the quantity of the food necessary to prevent or cure deficiency diseases. Hence the vitamine requirement may be estimated only in terms of the proportion of vitamine-containing foods required in the diet.

That the deficiency diseases are due to lack of vitamines can be determined only by the method of exclusion. Almost every imaginable cause has been attributed to the deficiency diseases, and some causes have been proposed that it is impossible for me to imagine. For instance, scurvy has been attributed to lack of ionization of the salts in the food due to staleness, and it is impossible for me to imagine a lack of ionization of these salts in food that has been eaten, and certainly food will not hurt you if you do not eat it. Scurvy has been attributed to an acid-forming diet, but McClendon, Cole, Engstrand and Middlekauff have shown that this factor is not responsible for scurvy. The germ theory of these diseases will probably be popular for a long time, since bacteria are always present, waiting for an opportunity to hasten the death of a weakened individual. It is therefore useful for purposes of discussion to include among deficiency diseases those that have been cured in the presence of a vitamin-rich diet and have not been cured in the absence of such a diet. We will consider deficiency diseases of infants and adults.

Rickets is perhaps the most common deficiency disease, frequently occurring in breast-fed infants. To quote a book written before Funk's ideas of vitamines were generally known, Miller states that, without doubt, rickets is to be regarded as a dietetic disease, and considers deficiency of butter fat as the most constant and potent cause. In treatment, among other things, he recommends milk, cream, butter, egg yolk and cod-liver oil. These fats are especially rich in the antirachitic vitamine. Since the bones are softened in rickets the child may not be able to take proper exercise or go out into the fresh air, hence the view that rickets is due to lack of exercise or fresh air. The mother's milk might be sufficient in antirachitic vitamine, and yet the child may have rickets, due to the fact that it was weaned too soon. The Fijians, who included some of the finest specimens of physical development in the human race, nursed their infants for three years, and as the mother's milk became deficient in quantity, supplemented it with bananas. Rarely a mother in this country nurses her children for three years, but in savage Fiji it was a religious custom, and the taboo was placed on the mother in order to prevent the interference of the father. The prevalence of rickets among negroes may be due to the fact that the mother's diet of corn bread and fat pork is deficient in antirachitic vitamine. The British Committee base their statements concerning rickets on the experiments of Mellanby on pups. Hess and Unger failed to cure rickety babies on cream, but did so on cod-liver oil.

Xeropthalmia, keratomalacia or *xerosis conjunctivæ infantum*, an eye disease of infants that has been especially prevalent in the Scandinavian and other European countries during the war, is due to lack of antirachitic vitamine, the deficiency probably being greater than that required to produce rickets. It is accompanied by diarrhea. Sztark cites a case that developed after an exclusive diet of pea soup for fifteen months, and was cured in ten days on a diet of cows' milk.

Infantile beriberi occurs in infants nursing from mothers who have the disease, and whose milk is consequently deficient in antineuritic vitamine.

Infantile scurvy is due to deficiency of antiscorbutic vitamine. To quote again from "previtamine literature" Miller states that the opinion most commonly held is that scurvy is caused by a diet which through sterilization has been deprived of its "fresh element" and recommends orange and grape juice in its treatment. The fact that scurvy may occur in breast-fed infants, indicates variations in the antiscorbutic content of milk.

Marasmus is often considered a dietetic disease. Miller states that not seldom the child has thrived on the breast for a month or two, and has then been weaned in order that the mother may go out to work, and from that time has gradually wasted. Eddy and

Roper claim that the addition of a powder rich in vitamines to the cereal food of marasmic babies increased tissue growth. Vitamines are certainly necessary for growth, but so are other food constituents.

Since the question of growth has been referred to, perhaps it is well to remember that for normal growth there is necessary not only vitamines, but also the secretions of ductless glands. It is well-known that the size of the ductless glands is greatly affected in deficiency diseases in man and animals. According to McCarrison, deficiency of vitamines in the diet leads to abnormalities in the secretion of the ductless glands. We know that iodin in the food is necessary for the normal functioning of the thyroid, and it is possible to imagine unknown constituents of the diet that may be necessary for the ductless glands.

Pellagra may occur in breast-fed infants whose mothers have the disease, but it usually takes a long time to develop.

Deficiency diseases of adults may be different from those of infants, because growth is complete, although many of these diseases characteristic of adults occur also during adolescence or infancy.

War edema, also called famine edema or hunger edema, has been ascribed to lack of the antirachitic or fat-soluble vitamine, or other element in the diet. The fat content of the diet in war edema is not accurately known, but Guillermin and Guyot state that the total ration was sometimes as low as 800 calories, and it contained a very small proportion of fat, and that a decrease of 40 per cent. in body weight was common. Park has shown that it is readily cured by a return to the normal diet. War edema, or famine edema, as it is more often called, is not a new disease. Lusk refers to an account of it in France in 1817, just 100 years previous to the late outbreak in Germany and other European countries and Mexico. He also states that cases were cured in a week by the addition of 100 grams of fat to the ration. It is stated that edema occurs when there is a decrease in blood-plasma proteins, and hence that decrease in protein in the diet may cause edema. A diet of 800 calories fed prisoners is naturally deficient in protein. The scorbutic symptoms observed by Beyerman in famine edema suggest scurvy or a complication of scurvy. He states that the edema was cured by adding vegetables to the diet. Edema occurs in various deficiency diseases, and hence some confusion may arise in the classification, but the large number of cases of war edema that have occurred recently, indicate that it is a separate disease. Schittenhelm and Schlecht observed decrease in blood proteins in war edema.

Beriberi is a form of multiple peripheral neuritis caused by a deficiency of antineuritic vitamine, and is most prevalent in rice-eating countries. Wet beriberi is accompanied by edema, but in dry beriberi this is substituted by atrophy. As is often the case

in deficiency diseases, there may be gastro-intestinal disturbances. The principal cause is too exclusive a diet of polished rice, and according to Fraser and Stanton, the substitution of undermilled rice, containing at least 0.4 per cent. of phosphorus, prevents the disease. It may be caused by too free use of any degerminated cereal. The addition of canned goods to the diet may not prevent it. There is apparently not enough yeast in bread to prevent beriberi. Beans and peas are perhaps the most useful preventives. In the treatment of the disease, extract of rice-polishings and fresh yeast or autolyzed yeast have been used. Funk, Lyle, McCoskey, Caspe and Poklop observed a mild glycosuria in man on a diet of white bread and polished rice.

Scurvy was perhaps the first deficiency disease to be recognized as such. Captain Cook showed that it could be prevented by the use of fresh vegetables. Nansen and Johansen passed a winter on an exclusive meat and fat diet without scurvy. Stefansson claims to have cured cases of scurvy by a raw meat diet. Apparently all fresh foods have traces of antiscorbutic vitamine. The juice of sweet limes or lemons is especially rich in this vitamine, and this fact has led to the development of a large industry for bottling lime juice. This preparation was not tested until recently, and was then found to be deficient. By some mistake, sour limes have been substituted for the curative sweet limes, and the lime juice of commerce does not come up to expectations.

Pellagra was called alpine scurvy by Italians, and has been shown by Goldberger to be a deficiency disease. By definition the disease is characterized by a symmetrical dermatitis, especially of those parts exposed to the sun, but this is not its most serious characteristic. The worst features of beriberi, scurvy and pellagra are the effects on the nervous system. The hemorrhages in pellagra are in the nervous system, whereas in scurvy they are general (and may occur in the meninges). Sundwall has shown that the tissue changes in pellagra are not specific, but are similar to those in animals on inadequate diets. In beriberi, pellagra and scurvy gastro-intestinal disorders are present. In pellagra edema is extremely localized, in scurvy it is associated with hemorrhage and in wet beriberi it is more general. Pellagra is of very wide distribution and may be worldwide. Since a patient with pellagra may live ten years, it is probably not due to complete absence of any dietetic constituent but to a slight deficiency. Whether this is a vitamine or an amino-acid, or both, has not been determined.

Trench foot is attributed by Bruntz and Spillmann to lack of vitamines associated with life in the trenches, the predisposing cause being the diet, and the water-filled trenches causing the acute symptoms in the feet.

Sprue was classed as a deficiency disease by Cantlie, who found scurvy in some cases. Brown states: "In the open alluvial workings

of a tin mine in the East Indies all of the employes are exposed to the same atmospheric conditions. The Chinese coolie is stricken with beriberi, his European overseer with sprue. In no essential condition, even in that of diet, are the circumstances of their daily life materially different. The treatment of sprue is essentially dietary. A milk diet, a raw fruit diet, a milk and fruit diet or a raw or rare meat diet is used. In any case the diet contains vitamines."

VITAMINES AND APPETITE. In all animal experiments on a vitamine-deficient diet loss of appetite occurs. With human beings, psychological factors may enter in so as to make it difficult to perform clean-cut experiments on this subject, yet the final loss in tissue substance in all deficiency diseases suggests that the appetite has been affected. We know that pure proteins, fats and starches have no taste, but we do not know whether vitamines have flavor. We do know, however, that the taste of milk changes on boiling and the taste of many foods changes by canning or drying. Why is it that some persons have been known to defy the cholera germ for a raw oyster and the typhoid germ for a salad, and to give their lives for a momentary tickling of the palate? There must be some great advantage in fresh foods or else the desire for them would be eliminated by natural selection. To the clothes-moth the age of food seems to make little difference, but when a man sits down to a meal of storage eggs, canned milk, jerked beef and hardtack it requires considerable hunger to whet the appetite. This craving for fresh food has probably saved more lives than are killed by germs. The human race has existed for some time prior to the advent of food chemistry, and most people live nowadays without the aid of that science. Unquestionably the appetite has played some part in the preservation of the race. It seems probable that the person who is presented with an adequate choice of natural foods from infancy will choose an adequate diet, and that the cause of the deficiency diseases is that an adequate choice of foods is not always supplied to the table. In the case of animals this question has been tested. Evvard allowed pigs free choice among a variety of foods, and in this way produced the largest pig for its age that was ever raised at the Iowa Experiment Station. A more rigorous experiment was made by Osborne and Mendel, since they did not use natural foods but purified components made into a biscuit. A rat presented with a more and a less adequate biscuit might eat for a few days from the less adequate, but finally showed preference to the more adequate diet. These experiments did not refer to vitamines exclusively, but they show that an inadequate diet results in some change in the appetite.

FOOD SUBSTITUTION. According to Steenbock, fat-soluble-A is more abundant in yellow foods than in corresponding white ones. Yellow corn contained more than white corn, yellow oleo oil more than white fat separated from the same adipose tissue, yellow

sweet potatoes more than white potatoes. The artificial coloring of butter may therefore deceive us as to its vitamine content. Without doubt the operation of the Pure Food and Drugs Act and the work of the laboratories operating under this law have been of inestimable advantage to the public. Food chemistry has not reached a sufficient stage of development to be relied on exclusively in questions of food substitution. Feeding tests are necessary, and the preference of the public for natural products, on which feeding tests have been made by the human race, is well grounded. The work of food fakirs has been insidious. Take the question of oleomargarin. The early products coming under this label in this country contained a large percentage of oleo oil, which is rich in the fat-soluble vitamine. Little by little the proportion of such oleomargarins has decreased and perhaps the majority of oleomargarins today are made from cottonseed and cocoanut oils and are deficient in fat-soluble vitamine. Galicians eat lard on their bread, but it is said that the black bread they use contains some fat-soluble vitamine from the rye germ. Negroes have a particular fondness for pork fat and white cornmeal bread, and this may be the chief cause of the prevalence of rickets in negro babies, since the diet of the mother does not contain enough fat-soluble vitamine to be transmitted to the milk. In a milk-canning factory in this country, skimmed milk and vegetable oils were run through a homogenizer and canned as milk compound. The cook may see the label on the artificial milk or butter, but the defenceless boarder does not even have the satisfaction of reading his sentence. Another deception is the soaking of dried green peas in water and then canning them. The Pure Food and Drugs Act does not allow the picture of a pea-vine to be placed on these cans, but the average consumer is not familiar with such distinctions in labels.

In natural foods a sweet taste is associated with fruits that are rich in antiscorbutic vitamines. If we may suppose that the taste for sweets is inherited, our savage ancestors may have eaten raw fruits, just as the monkeys in the jungle do nowadays. Most of the sweet food and drinks of modern man are made from sugars and molasses and honey that are free from vitamines. Coffee and its substitutes and tea, malted or distilled liquors, wines and carbonated drinks with synthetic flavors are deficient in vitamines.

I ordered a meal in a "pure food restaurant" and received various fake dishes, including an imitation beafsteak made of degerminated cereals. The fact that we use milk with cereals is probably what saves us from disaster. One is reminded of the old story of the soup-stone: A man knocked at the kitchen door and said he was introducing soup-stones. The stone was to be boiled in water, and he demonstrated it to the housewife, suggesting various ingredients that might be added to it. These were promptly produced by the enthusiastic housewife and the man drank the soup,

leaving her the stone. Cereals form the basis of our diet, but scurvy develops when they are used as substitutes for potatoes or other vegetables, as occurred in Glasgow, Newcastle and other cities during a potato shortage during the war. In one institution in the United States there were 200 cases of scurvy on April 1, 1916, following two months' reduction of the potato and other vegetable ration to one-half.

THE MILK QUESTION. The rise in the cost of living, more than the rise in the cost of milk in particular, has led to a reduction in the consumption of milk by families with small incomes. Harris records data from 2084 families, representing in nationality and income a typical cross-section of New York City in the summer of 1918. In 14 per cent. of these families milk was entirely eliminated from the children's dietary. McCollum has repeatedly emphasized the advantage of milk in the diet. Mendenhall states that every child from eighteen months to twelve years of age is better for having one and a half pints of milk in its daily diet, and that fluctuations in the demand for milk or diminished use of milk throughout the country will inevitably result in a lessened production, and that the loss of our herds at this critical period would be a calamity. Hart and Steenbock call attention to the use of milk as a supplement to cereal foods. Milk makes up the deficiency of cereals in vitamines, salts and certain amino-acids of the proteins. The United States Food Administration calls attention to the fact that milk compares favorably with other animal foods in price per gram of protein and in price per calorie, and that there is only enough milk consumed in this country to give each person a little more than half a pint per day. Twenty and more years ago a professor of mathematics used to tell a story of being hard up in his college days. He calculated that he would have ten cents a day to spend for food, and that the highest nutritive value could be gotten from ten cents' worth of milk. Practical experience, however, suggested a change to five cents' worth of milk for nourishment and five cents' worth of mince pie to "stay with" him.

The chief value of milk lies in the fact that it is a complete food and does not require any balancing of components or any precautions to include the minimum requirement of any constituent. I have never found a species of cooks who would calculate or weigh or balance any food constituents except under immediate compulsion. With a milk diet for the infant and a modicum of milk in the diet at all other ages the expense of calculation of dietary constituents is eliminated, and milk even at a high price may be worth buying in order to avert the danger of malnutrition and doctors' bills or loss of efficiency. It is an open question, however, whether cows' milk has been beneficial to infants in general. During the famine resulting from the siege of Paris the infant mortality fell 40 per cent., due to the fact that mothers nursed their own infants. A similar

decrease occurred during the great Lancaster cotton famine, due to the fact that the mothers could not work in the factories and did not have the money to buy cows' milk for the infants. During the recent occupation of Lille by the Germans, when the adult population lost about 40 per cent. in weight, there was a reduction in infant mortality, due to the fact that the mothers nursed their own infants. In the absence of mothers' milk, however, cows' milk is the best food for infants, but it is better to feed the cows' milk to the mother if she can nurse her child.

ARMY RATIONING. It seems probable that the chief point of attack of faulty nutrition on the military strength of a nation is on the infant males. Crooked bones, bad teeth and other deficiencies may result from faulty feeding of prospective soldiers. If the soldier going into action has a well-nourished body to begin with a short campaign on very defective rations may not lead to serious consequences. The protein, fat, mineral salts and vitamines stored in the body may be drawn on to make up the deficiency. It is often stated that the body cannot store protein, and it is true that protein is not stored in the same way that fat is; but the protein of the muscles may be drawn on for a considerable period, as has been the case in millions of persons during this war.

The ration allowed the army by Congress has been subject to many variations. The soldier eats what he can get, but must necessarily be influenced by the ration allowance. During the Revolutionary War conditions were very variable. In 1780 the American Army was increased by the addition of the French Division (5000 men), who landed from transports with over 600 cases of scurvy among the soldiers and 1000 cases among the sailors after a voyage of two months and nine days.

In 1775 fresh milk was included in the army ration, but since it could not always be supplied a revision of the ration was soon necessary. In 1798 Congress fixed the ration at 20 ounces of beef, 18 ounces of bread and an allowance of salt, soap and candles. Food profiteers made a liberal interpretation of the words "bread and beef," so that the Surgeon-General thought it necessary to report unfavorably on the results. The two staple articles of the ration have remained practically unaltered in quantity until the present day, but later Congresses allowed liquor and specified substitutes for beef. In 1818 the President was authorized to make changes in the ration other than increase in cost, and in 1834 he substituted coffee and sugar for the liquor component. Temporary increases for the period of the Civil War were made, but except when raids were made on food stores the nutrition of the troops was not ideal. Owing to the large proportion of preserved food, including flour, salt meat, desiccated vegetables, canned milk and coffee extract, 30,741 cases of scurvy were recorded among white troops. In 1890 a pound of fresh vegetables was added to the ration

and in 1908 the present garrison ration was authorized, which is of sufficient cost and allows sufficient substitution to furnish an adequate diet. The savings privilege in rationing in garrison, authorized in 1910, was abused to such an extent that it was discontinued April 1, 1919, and all substitutes are purchased through the quartermaster and the savings revert to the Government.

About the only data we have of the nutritive balance of our soldiers are their weight records. According to Munson the average peace-time recruit gains about 2.8 pounds in the first three and a half months of military service. Similar figures for the National Army, compiled by Hildebrandt, show a gain of 6.4 pounds in the first four months of military service. The total gain during the war has been reported as twelve pounds per man. Such figures are encouraging, considering the fact that some of the recruits were undernourished at the time of enlistment. If the added weight is not necessary for muscular strenght it is useful in raising the resistance to disease and famine. The army has experimented with an emergency ration, consisting of a dried mass of chocolate, eggs, milk and sugar that has a high protein and calorific value, but no one has been able to eat it for more than three successive days. When water only is available a reduction of a pound a day in body weight occurs in warm weather and more as the weather turns colder, and a few pounds excess body weight form the best emergency ration, since accidental loss is eliminated. Owing to the fact, however, that carbohydrate is stored to a very limited extent in the body, the use of hardtack, if available, is advantageous.

I have had opportunity to compute the protein, fat, carbohydrate and total calories per man per day in a large number of army messes and have studied the data compiled by the Food Division, and in the majority of the few cases of deficiency noted, have found that the mess sergeant was inaccurate in his accounts or was trying to produce an impression on the inspectors. In some cases the soldiers and their mess officers complained of the food. The chief ground of complaint was that there was not a sufficiency of fresh fruit and vegetables. I computed the mineral constituents, and especially the acid-base balance, of these messes, and found them usually acid. Certain foods, however, which yield a basic ash (dried beans, for instance) were served too frequently to please the soldiers. It was not the character of the ash of the food which influenced their comment, but its freshness. Certain national guard companies had company funds sent them from their home towns. I found some of these companies at Camp Cody, N. M., spending thirty cents per man per day for fresh milk and a more variable sum for fresh California fruit. A certain officer having about 2200 men in his command found inefficiency in one or more of his mess sergeants and decided to run the messes himself. He made up bills of fare for twenty-one meals and ordered all mess

sergeants in his command to use them. The foods listed were those carried by the quartermaster and there was a conspicuous absence of the fresh fruits and vegetables of the local markets. I found the order to use the menu evaded more frequently the farther the mess was from headquarters, and at the end of ten days the scheme was abandoned. If the desires of the soldiers may be expressed in chemical terms, they desired vitamines, and especially antiscorbutic vitamines.

Whereas the ration allowance for soldiers on duty has been based on the price of food, and the same was originally allowed for sick soldiers, during a certain period each base hospital was allowed a fixed sum of money for each sick soldier on its rolls. On June 1, 1918, the ration allowance for a sick soldier was fixed at fifty cents. In some of the larger hospitals savings were made, but the smaller hospitals reported that the allowance was not sufficient. I have no records for the same hospital covering a long period, but by combining data from three hospitals some comparisons may be made. These data are from Camp Pike, Ark., June, 1918, Camp Cody, N. M., August, 1918, and Camp Fremont, Cal., November, 1918. During this period there was a general rise in the cost of food, and to meet this, reductions in the higher priced articles of food were made. In June 13 ounces of fresh meat per ration were served, in August 7 ounces and in November only 3.2 ounces. In June 2.5 eggs per ration were served, in August 1.2 and in November 0.4. At Camp Fremont from August 1 to September 1 the rise in price of fresh eggs was from 52 to 89 cents per dozen, of fresh milk from 23 to 40 cents a gallon and of oranges from 6 to 13 dollars a crate. At the end of this period the fixed allowance was superseded by a sliding scale system based on the local cost of the garrison ration plus a certain percentage that was greater the smaller the hospital.

The above remarks apply to the army in this country, but the United States troops in other countries have not always fared so well. Beriberi among the Philippine scouts gave occasion for an order that the meat ration was to be eaten and that the rice was to be undermilled (Chamberlain). Riddell, Smith and Gutierrez reported 60 cases of beriberi in the United States Army in Porto Rico November, 1918. Potatoes, beans and canned meats and vegetables were supplied the troops, and these data led to the supposition that the reduction in vitamine by canning may have been a factor.

The fly problem is serious in the army. Ball has shown that the house-fly may be carried 100 miles by the wind. I have seen squads of soldiers swatting flies in mess halls when the civil authorities allowed a mountain of horse manure to remain two miles outside of camp.

Discussion. Observations, some of which are reported in this paper, have led me to believe that the nutrition of some individuals,

especially infants, is not ideal, and that the high cost of living is leading to worse nutrition. A large part of the population has unconsciously depended on the presence of milk in an otherwise inadequate diet, and the decrease in milk consumption that is now taking place is to be viewed with alarm. The supply of fresh green vegetables is not sufficient to be a substitute for milk. Grass is not adapted to human alimentation except in the form of sprouted grass seeds. In the sprouting of seeds vitamines are syntheized in the young leaves and a quick crop of vitamines may be obtained without the necessity of planting the seeds in the ground. McClendon, Cole, Engstrand and Middlekauff have most recently studied the question of sprouting cereal grains. Wheat or rye, sprouted until the shoot extends an inch beyond the grain and heated in water to 70° to gelatinize the starch, forms a cheap and convenient and palatable source of vitamines. The seeds may be freed from bacteria before sprouting (Braun and Duggar and Davis). Since beef fat is about as valuable a source of vitamine as butter is, beef drippings and fat should be eaten rather than thrown in the garbage can, and the same applies to some other animal fats. Prolonged cooking of fresh foods should be discouraged, but all canned goods should be heated to boiling before serving, in order to destroy toxins of Bacillus botulinus that might be present, unless a competent inspection of the goods has been made.

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THE CURE OF HOOKWORM INFECTION.[1]

By John L. Kantor, M.D.,
CHIEF IN DIGESTIVE DISEASES, VANDERBILT CLINIC, COLUMBIA UNIVERSITY, NEW YORK CITY.

During the recent war there were admitted to the author's gastro-intestinal service at the United States Army General Hospital No. 14, Fort Oglethorpe, Georgia, 393 cases of ankylostomiasis, over one-fourth of which had received previous and obviously unsuccessful hookworm treatment. This large proportion of failures is due, in our opinion, (1) to the real difficulty of achieving a complete cure quickly by the methods of treatment heretofore in vogue, and (2) to the lack of sufficient observation after treatment, owing in turn to the absence of satisfactory scientific data on which the precise criteria of cure could be based. It has been our endeavor to remedy both these defects, the former by the development of the intra-intestinal tube treatment already described[2] and the latter by means of the most intensive studies of the results of therapy that we could possibly make under army conditions.[3]

As soon as a hookworm suspect was admitted to our service, and before any treatment was given, stools were sent daily to the laboratory until the diagnosis was confirmed beyond question. After treatment, specimens were similarly examined, every other day, as a rule, until an interval of twenty-eight days had elapsed, unless they were reported positive before that. For the purpose of compiling the statistics presented in this paper, all incomplete observations have been entirely discarded. Our conclusions, accordingly, are based on 231 cases, all of which were observed twenty-nine days or over (up to two hundred and twenty-eight

[1] Read before the Duval County Medical Society, Jacksonville, Fla., Oct. 28, 1919.

[2] Kantor, J. L.: The Intra-intestinal Tube Treatment of Hookworm Infection, Jour. Am. Med. Assn., 1919, vol. lxxiii, 1181.

[3] At the time this work was carried on, Lieut.-Col. Calvin D. Cowles, Jr., of the regular army, was in command of the hospital. Dr. Lewis C. Ecker, of Washington, D. C., was in charge of the medical service. Drs. Burrill, Dunning, Paul, Hill, Hughes, Swan, Hagler, Rudbeck and Mahoney were at various times associated with the gastro-intestinal section. Dr. Le Roy Smith was in charge of the laboratory. The actual stool examinations, a task of great magnitude, were very capably performed by Mr. E. A. Piper.

days in one instance), and no case is reported as a cure that did not show an average of ten to fifteen consecutive negative stools during a period of four weeks after treatment. Some of the cured cases we were able to follow for a much longer time, one soldier having his twenty-fourth negative stool one hundred and thirty-six days after treatment.

The first problem that engaged our attention in a preliminary way was the absolute diagnosis of the existence or absence of infection in a given case. Thanks to Kofoid and Barber's loop-flotation-brine method of examining stools for ova,[4] an extremely delicate laboratory procedure was already at our disposal. We accordingly endeavored to determine how many negative stool examinations should be demanded before a given Southern soldier could be pronounced hookworm-free. Obviously a single examination could not reasonably be expected to reveal every infection either because of errors unavoidable in a large series, because of very slight infections or because the worms were not constantly ovulating. The question was really one of importance not only because we had to be sure of our control methods, but because the reinfection of any case, treated or untreated, had to be taken into consideration. With these objects in mind it was arranged that all Southern soldiers admitted to the *medical* service of the hospital for the period of one month were to have their stools examined five times (on approximately five successive days) or until positive, whereas all patients admitted to the *surgical* service during the same period were to have but a single stool examination. As a result, of the 408 medical cases examined, 63 were found positive after the first stool, 17 more after the second, 12 more after the third and 3 more each after the fourth and fifth—a total of 98 positive cases, or 24 per cent. of the number examined. On the other hand but 32 of the 231 surgical cases were found positive with the single stool method, a percentage slightly under 14. In other words the five-stool method gave an increased incidence of over 9 per cent., and an increased efficiency (as between the two methods) of almost 40 per cent. To crystallize the importance of this, we found that one-quarter of the returning troops were still hookworm-infected by the five-stool method, whereas but one-seventh of the men would have been pronounced positive by a single stool examination.

In this connection it should be stated that the procedure recommended above is designed to reveal infections only in untreated cases or in those whose last treatment took place at least six weeks or two months before the examination. It is of course well known that vermifuges have the property of depressing the egg-laying function of parasites, but the exact duration of this "negative phase" in the case of the female hookworm seems to be a matter of uncertainty.

[4] Kofoid, C. A., and Barber, M. A.: Rapid Method for the Detection of Ova of Intestinal Parasites in Human Stools, Jour. Am. Med. Assn., 1918, lxxi, 1557.

In order to throw more light on this interesting question an analysis is presented of 100 cases which were reported positive after having received treatment on this service. (See Table I.) The drug used was oil of chenopodium in doses averaging 3. c.c. by tube and 2 c.c.

TABLE I.—SHOWING DAYS ON WHICH STOOLS FIRST BECAME POSITIVE AFTER 100 UNSUCCESSFUL HOOKWORM TREATMENTS.[5]

Days after treatment.	No. of cases positive.	Weekly total percentage.
4	18	
5	19	
6	13	1st week, 61
7	11	
8	3	
9	3	
10	4	
11	1	2d week, 81
12	4	
13	2	
14	2	
15	2	
16	2	
17	1	
18	1	3d week, 90
19	1	
20	2	
21	1	
22	2	
23	2	
24	0	
25	2	4th week, 98
26	1	
27	1	
28	0	
29	0	
30	1	
31	0	
32	0	5th week, 99
33	0	
34	0	
35	0	
36	0	
37	0	
38	0	6th week, 100
39	0	
40	1	

by mouth in capsules. Stools were examined every other day, and in many cases daily, until they came back positive or until an interval of at least four weeks had elapsed after the day of treatment. Since the roentgen ray and other means of studying bowel-emptying have shown that it may take up to seventy-two hours

[5] Positive results within the first three days are disregarded. See text.

for the complete evacuation of a given meal, an arbitrary three-day limit was established, on the assumption that this would be sufficient for the discharge of all ova produced by worms that had been destroyed by the vermifuge. Accordingly, in the case of stools reported positive within this limit judgment as to cure or failure to cure was suspended until this interval was passed. Subsequently, if the positive results persisted, the case was pronounced uncured; or, if the stools remained negative *for at least four weeks*, the case was called cured. In every instance the period of four weeks was reckoned from the last positive stool, the total observation interval being thus lengthened to thirty-one days when the stool came back positive on the third day after treatment. It will be seen from a study of the accompanying table that observation for four weeks is by no means too long if one wishes to know whether a cure has acutally resulted from a given treatment. As it is we have records of 2 cases which became positive only in the fifth and sixth weeks respectively, and by no means all our cases were observed for so long a period. In brief, 98 per cent. of our positive cases (or failures to cure) became such within four weeks, 90 per cent., within three weeks, 80 per cent., within two weeks and only 61 per cent. within the first week. It follows that an individual reported as negative within the first week after treatment may have more than one chance in three of coming back positive at some subsequent examination. That many cases were erroneously considered cured after a routine hookworm treatment as carried out in the various army organizations goes almost without saying. Moreover, when the question of reinfection arises one must be particularly careful that the original disease was actually cured in the first place.

In this connection we should like to point out still another possible source of error in diagnosticating the cure of hookworm infection. In their extensive study of this disease in the Orient, Darling, Barber and Hacker[6] presented a method for grading the value of any particular form of hookworm treatment by comparing the number of worms removed by a first treatment with the total number of worms removed by subsequent treatments. This method was further developed into an "efficiency index" by Knowlton working in Kofoid's service.[7] Admirable as this procedure is for a comparative study of treatment methods it should by no means be translated into a criterion of cure for the disease, the weak point in the efficiency index method being that further examination of stools presumably ceases as soon as any particular treatment fails to reveal the presence of worms in the excreta. As already explained in the author's previous communication all forms of treatment by mouth have the common objection that the vermifuge is not delivered directly at the site of infection. Hence the chance of

[6] The Treatment of Hookworm Infection, Jour. Am. Med. Assn., 1918, lxx, 499.
[7] Knowlton, R. H.: Hookworm Infection among Troops, Ibid., 1919, lxxii, 701.

missing the worms partially or even entirely is by no means merely academic. The following case is cited as an example:

CASE B 208.—Had three treatments, presumably by thymol, before entering the army.

Fourth treatment February 26, 1919, 2 c.c. oil of chenopodium in freshly filled hard, gelatin capsules. *Eighty worms recovered* from resulting stools. Subsequent stools positive for ova for eight days.

Fifth treatment, March 7, same as fourth, *eighteen worms recovered*. Subsequent stools positive on fifth and seventh days.

Sixth treatment, March 18, same as previous, *no worms recovered*. Stools, however, positive on second, third and sixth days.

Seventh treatment, March 27, same as previous *no worms recovered*. Stools positive on second, fourth and sixth days.

Eighth treatment, April 5, same as previous, *twenty worms recovered*. Stools negative for eight days more, at which point observation discontinued. Final result undetermined.

We were again and again impressed with this failure to cure after any of the usual forms of mouth treatment. Indeed, the same conclusion is reached from a study of any of the more careful work that has been reported in the literature. Thus in the severer types of infection encountered by the original Porto Rico Commission[8] the majority of cases were not cured before four doses of anthelmintic had been administered and there are examples of twenty-two, twenty-three and twenty-five treatments being given without curing the infection. More recently the International Health Board, after a four years' intensive campaign in the West Indies,[9] is able to report only 50 per cent. of cures after two treatments. Our own experience with the mouth treatment of the relatively mild infections found in the army was not very encouraging. Of the 87 cases treated by the mouth method (2 c.c. oil of chenopodium in freshly filled hard capsules) we could prove a cure in only one-half, this notwithstanding the fact that each man was observed and treated for a period of four weeks or more. If still positive at the end of this observation the patient was either discharged uncured or given tube treatment. As a matter of fact, 5 cases were still positive after six treatments, 3 after seven and 2 were left doubtful (owing to insufficient observation) after eight.

On the other hand our experience with the intra-intestinal tube method convinced us of its superiority over the usual forms of mouth treatment as a means for the rapid and complete eradication of hookworm disease. Of 137 cases treated by the tube we were able to prove a cure, despite the difficulties in observation, in over 87 per cent. Perhaps still more noteworthy is the fact that fully

[8] Ashford, B. K., and Igaravidez, P. G.: Uncinariasis in Porto Rico, Senate Document 808, Washington Government Printing Office, 1911, p. 162.

[9] Howard, H. H.: The Control of Hookworm Disease by the Intensive Method, Publication No. 8, Rockefeller Foundation, New York, 1919, p. 75.

80 per cent. were cured by the first treatment as compared with 34 per cent. by the mouth method. Furthermore, although the mouth method failed in our hands after even a sixth and seventh repetition only one tube case had to go on to a third treatment, the rest being cured in one or two sessions.

TABLE II.—SHOWING COMPARATIVE RESULTS OF MOUTH AND TUBE TREATMENTS.

Treatment.	No. of cases.		Percentage cured separately by each treatment.		Percentage uncured of all cases.	
	Mouth.	Tube.	Mouth.	Tube.	Mouth.	Tube.
1st treatment	35[10]	137	43	**80**	86	**19.0**
2d treatment	70	10	18	**90**	65	**0.7**
3d treatment	37	1	32	**100**	29	**0**
4th treatment	14	..	21	..	17	
5th treatment	9	..	11	..	9	
6th treatment	5	..	0	..	6	
7th treatment	3	..	0	..	2	
8th treatment	2	..	?	..	?	

It remains to point out still another advantage of the tube technic. It will be observed, by referring again to Table II, that 34 per cent. were cured by taking the first mouth treatment, 18 per cent. by the second, 32 per cent. by the third, 21 per cent. by the fourth, 11 per cent. by the fifth and none at all by the sixth, seventh and eighth. In other words the chances of being cured became progressively less hopeful as treatment was continued. This result is undoubtedly due to errors residing in the rationale of the mouth method, the reason for the fifth failure being just as great as for the first. Such a persistent disappointment might, for example, be due to the patient having achylia gastrica, in which case the associated hypermotility might carry the capsule far into the ileum before its dissolving. On the other hand the soundness of the principle underlying the tube treatment is further vindicated by what might be called its cumulative efficiency, 80 per cent. of the first treatments being successful, 90 per cent. of the second and fully 100 per cent. of the third.

Encouraged by the above experience the author feels justified in recommending the tube method as worthy of trial by the profession. Two treatments, given a week apart, should be sufficient to cure most cases. At first the method should undoubtedly be used only in hospitals, whether civil or military, or in the homes of patients.

[10] Most of the previously *untreated* cases were given tube treatments, hence the relatively small number of first mouth treatments. On the other hand, almost all the previously *treated* cases were given mouth treatments with the exception of a few not included in this table.

After its safety and usefulness are further demonstrated by added experience, and perhaps after appropriate modifications and improvements in the technic, it may not be too much to hope that the tube treatment will ultimately become the method of choice in the eradication of hookworm infection.

SUMMARY. 1. An individual from a hookworm district should not be pronounced hookworm-free until a series of at least five negative stools has been obtained, and then only if the last treatment took place six weeks or more previously.

2. The "latent period" after treatment, *i. e.*, the period in which the egg-laying function of the hookworm is depressed by the vermifuge so that the persistence of worms cannot be revealed by stool examination, may extend up to six weeks. However the great majority (98 per cent.) of cases become positive again within four weeks after treatment.

3. The usual form of treating ankylostomiasis with drugs given by mouth has been shown to be unsatisfactory, even relatively mild infections resisting as many as seven or eight treatments.

4. Much more efficient results can be obtained by the method of intra-intestinal tube treatment, owing to the fact that the full, concentrated dose of vermifuge is delivered precisely at the point of infection. Instead of 34 per cent. of cures, as in the case of a first mouth treatment, fully 80 per cent. are cured by a first tube treatment. Only one repetition is necessary for the relief of the great majority of infections.

THE TREATMENT OF CATARRHAL JAUNDICE BY A RATIONAL, DIRECT AND EFFECTIVE METHOD.[1]

BY B. B. VINCENT LYON, A.B., M.D.,

CHIEF OF CLINIC, GASTRO-ENTEROLOGICAL DEPARTMENT, JEFFERSON HOSPITAL; ATTENDING PHYSICIAN, METHODIST HOSPITAL, PHILADELPHIA, PA.

I DESIRE to present in this paper a rational, direct and effective method of treatment of catarrhal jaundice. I say a direct method to draw attention to the contrast between it and the usual symptomatic or expectant plan so commonly employed in treating these cases.

I will limit my subject to the treatment of catarrhal jaundice by this new method, with a passing allusion to the treatment of other more important conditions of the biliary tract.

The diagnosis of catarrhal jaundice, as a rule, does not offer

[1] Read before the Philadelphia Clinical Association October 27, 1919. This is the second of the series of articles on the diagnosis and treatment of diseases of the biliary tract.

many difficulties. This type of jaundice usually develops in a young person and more often in young men than in women. There is frequently a history of several days or weeks of a preceding gastro-intestinal disturbance, which with careful questioning can be traced to some definite cause. The patients are often conscious of the gastric discomfort, evidenced by epigastric distress and soreness after eating and associated symptoms of bad taste, furred tongue, increasing constipation, sour eructations, belching and flatulency. The jaundice appears gradually, usually noticed first in the whites of the eyes, often first called to the patient's attention by other people. Later there is a gradual deepening of the jaundice elsewhere. Less frequently the jaundice appears rapidly, almost overnight. The degree of jaundice varies in proportion to the catarrhal swelling of the common duct and the consequent degree of obstruction to the exit of the bile into the intestines. Even when the jaundice is extreme the symptomatic discomfort is relatively slight; increasing lethargy, mental hebetude, drowsiness, distaste for food and occasionally soreness over the liver. In the deeper states of jaundice itching of the skin may be troublesome and occasionally patients may complain of "seeing yellow." As a rule this is all. When in addition there is complaint of feverishness and chilliness and more definite pain there is probably infection plus catarrh. There is generally noticed jaundice, furred tongue, sore epigastrium, sometimes an enlarged liver, perhaps sore to heavy percussion. It is seldom that the gall-bladder is palpable or the spleen enlarged. The pulse is generally slow and the temperature is normal or subnormal. Objectively, too, we notice the bile-stained and scanty urine and the stools seemingly acholic. I say seemingly because on chemical and microscopic examination of the stool we may find that bile is coming through, although in lessened amount, and the pale, pasty appearance of the stools is due to the failure of fat digestion. Fermentation of the stool may be conspicuous and the odor is sour and offensive. Constipation is the rule, but there may be diarrhea due to the gastro-enteritis. The blood picture is normal, as a rule, except when the catarrhal jaundice is complicated by an already existent anemia or infection. The only constant abnormal phenomenon is the prolongation of the coagulation time. Cabot[2] calls attention to the frequency of the loss of weight that occurs during the course of many cases. This has not been conspicuous in the cases here reported. This is the picture of catarrhal jaundice. The diagnosis is usually confirmed by the benign course which rarely exceeds six to eight weeks even in untreated cases and the majority terminate in recovery. I do not intend to enter into a discussion of the differential diagnosis between "simple" catarrhal jaundice and the jaundice designated toxic, infectious,

[2] Differential Diagnosis, Philadelphia.

epidemic or metabolic, nor to discuss the validity of the so-called entity of Weil's disease nor to reopen the controversy between hepatogenous and hematogenous jaundice. It is interesting, however, to see the increasing tendency to consider jaundice, of whatever type, of hepatogenous origin. I do not desire to discuss the various avenues of infection of the biliary apparatus and their relative frequency. Suffice it to say that the gall-bladder and ducts may derive their infection through the portal veins, through the systemic blood, through the lymphatics, through the serosa from direct contact with infected neighborhood peritoneum, and finally by direct ascending infection of the common bile duct from the duodenal zone. I do desire, however, to emphasize the frequency of this last avenue of infection in catarrhal jaundice, based upon the study of this and other groups of cases.

For the proper understanding of the various conditions and infections of the biliary tract, reference is directed to the discussion of the subject by A. O. J. Kelly[3] in his Mütter Lecture, delivered in 1905. An able article on epidemic jaundice has been contributed by Barker and Sladen.[4] Their attached bibliography will serve to amplify our knowledge of this interesting condition. It is instructive to delve into the history of jaundice.[5] The literature is simply voluminous, but we refer particularly to the monograph on jaundice by Harley,[6] published fifty-seven years ago, the clinical lectures by Sir Henry Marsh,[7] and to the exhaustive monograph of Legg, entitled *The Bile, Jaundice and Bilious Diseases.*[8]

My special concern is to bring forward a method of rational, direct and effective treatment of catarrhal jaundice. To treat disease intelligently and effectively we must have a rational conception of the life history and etiological and pathological factors of each given disease modified by an appreciation of the histology and anatomy of the tissues diseased. Our present conception of the pathology of catarrhal jaundice is that it develops from the extension of a gastroduodenal catarrh, passing upward into the terminal portion of the *pars intestinalis*, causing edematous swelling and congestion, and an increased production of mucus in the common bile duct, with often a plug of inspissated mucus corking up the ampulla of Vater. Owing to the exceeding rarity of deaths from catarrhal jaundice our opportunities to verify this conception at the postmortem table have been limited. Osler,[9] however, observed a case which at autopsy showed the common bile duct obstructed with inspissated mucus at its terminal portion and slightly distended above. The hepatic duct

[3] Am. Jour. Med. Sc., September and November, 1906.
[4] Johns Hopkins Hosp. Bull., October, 1909, xx, 223.
[5] Toxic Jaundice, Proc. Royal Soc. Med., October 1, 1916–1917.
[6] Jaundice, the Pathology and Treatment, Walton and Maberly, London, 1863.
[7] Clinical Lectures, London, 1867, vol. i.
[8] Legg, J. Wickham: The Bile, etc., New York, 1880.
[9] Practice of Medicine.

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was also distended. More recently Eppinger[10] described such an autopsy in which it was found that the occlusion of the common bile duct was due to a hyperplasia of the lymphoid tissue of the ductal mucosa, especially in that fraction of an inch which runs diagonally within the wall of the duodenum. He also found dilatation of the biliary ducts above this point. Eppinger and others believe that this lymphoid tissue acts as a defensive mechanism against infection, as does the lymphoid tissue in the tonsils, the bronchial lymph glands, the appendix, etc. The swelling, congestion and edema and mucous catarrh may progress higher in the common duct and into the cystic and hepatic ducts. This doubtless occurs in the cases of catarrhal jaundice of more prolonged duration, for it is easily conceivable that duration of the jaundice may run parallel to the extent as well as to the degree of duct catarrh. And what is the etiological factor primarily responsible for this catarrh? A catarrhal gastritis and a catarrhal duodenitis! There are no doubt mild cases of jaundice produced by pressure effects on the ampulla of Vater from edematous swelling of the duodenal mucosa alone without an extension of the catarrh into the duct itself. But what precedes the gastroduodenal catarrh? Surely dietetic indiscretions, exposure to cold and internal chilling and infection. I think we will find this true more and more frequently as we study our patients more closely.

Sixteen cases of catarrhal jaundice were observed and treated by me in Naval Base Hospital No. 5 in Brest, France, and were derived from officers and enlisted men chiefly engaged in destroyer duty. The destroyer service is always difficult enough in itself, but in patrol duty on the Brittany coast and in the Bay of Biscay in winter the weather is always cold and damp and the sea is rough. Some suffered exposure to cold and the chilling from sea-soaked clothes for many hours at a time. Tonsillitis and rhinitis were frequent and bronchitis and bronchial colds were the rule and there was also epidemic and pandemic influenza. As to dietetic indiscretions; in the destroyer flotilla on sea duty and especially in war time there is no such thing as dietary discretion. Rarely is there opportunity to eat hot or fresh cooked food, except soup and beans. The men eat standing, and hastily gulp their food. Can this predispose to gastroduodenal catarrh? In addition there is the sea-sickness, with its local pathology of a congested and erosive gastric mucosa. Now reconsider what I have just said in regard to the frequency of tonsillar, bronchial and influenzal-pneumonic infections, with the swallowing of infected material from the mouth and respiratory tract. The microörganisms are furnished and the potential etiological chain is complete. We proved nearly 100 cases of infective gastritis and duodenitis in one base hospital alone and in scores of postinfluenzal cases that I have

[10] Wien. klin. Wchnschr., 1908, xxi, 480.

seen and examined since my return during the past ten months. Sixteen cases of catarrhal jaundice among these 100 is a high percentage.

Analyzing these cases I find that one occurred in a man with a pronounced oral sepsis; one in a man following intensive syphilitic treatment, oral and intravenous. Two cases occurred within a week after operations on the nose and throat, one a tonsillectomy and the other a septum repair. Four were postinfluenzal infective cases and 8 of these 16 cases occurred in men serving in the "Black Gang," that is, in the fire or engine room, below decks, where they had to swallow their infected salivary or bronchial secretions on account of naval discipline. One of these 8 cases gave a history of acute catarrhal jaundice four years previously. Possibly this case should be excluded on the ground that it was a reëxacerbation of an antecedent cholecystitis or cholangitis. But I am including it because both the histories of the first attack and the one which I observed were clearly that of simple catarrhal jaundice, and because I believe that catarrhal jaundice, simple and benign as it is, is pregnant with possibilities of future and more serious disease of the biliary tract and may prove to be a direct starting-point for some cases, perhaps more than we now realize, of cholecystitis, cholelithiasis and choledochitis. In the near future I purpose reviewing a series of catarrhal jaundice cases and to institute a "follow-up" on them to ascertain the frequency (or infrequency) of subsequent disease of the biliary apparatus.

Of these 16 cases all of them gave proved evidence of gastroduodenal catarrh plus infective gastritis, infective duodenitis or both. Nine of these cases, the first observed, were treated after the manner of the usual symptomatic or expectant plan: Bed rest; diet restricted to proteins and fats; calomel and Epsom salt courses; later other cholagogues, such as blue mass, podophyllin, aloes, etc.; sodium phosphate in hot water on the fasting morning stomach; urotropin; the salicylates or fel bovis; gastric lavage; during convalescence nitrohydrochloric acid and nux vomica or other tonics. It has been stated that cold colonic irrigations stimulate the intestinal stasis and may stimulate gall-bladder peristalsis. I have not personally tried them, but it seems to be empirical and irrational therapy. The average duration of these first 9 cases so treated was thirty-five days before the jaundice had completely cleared.

In a second group of 7 cases, because our hospital facilities were improved and because some special duodenal apparatus had arrived, I adopted the plan of treatment I now desire to advocate. At the first visit to each patient I ascertained the possibility of antecedent mouth or respiratory tract infection and then proceeded to ascertain the presence of catarrhal or infective processes in the stomach and the duodenum by examining both fasting and digesting secretions from both of these zones, chemically, microscopically and bacterio-

logically, with the help of Dr. Hugo, our pathologist. I was thus able to prove the presence not only of a gastroduodenal catarrhal inflammation but also the local implantation of pathogenic microorganisms either in the stomach or duodenum alone or at both places. Among the bacteria recovered and identifiable were streptococci, staphylococci, Micrococcus catarrhalis and pneumococci in both the stomach and duodenum, and in the latter bacilli of the colon group. This gave a lead as to rational treatment. All patients, whether with bronchial conditions or otherwise, were cautioned repeatedly against the swallowing of saliva; noses were sprayed with Dobell's solution; throats gargled with strong potassium permanganate solution, 1 grain to the ounce. A sterile duodenal tube was passed to the stomach in the fasting morning state, the residuum withdrawn for analysis and microscopy, with a sterile individual syringe for each patient. The stomach was washed with water, followed by liquor antisepticus alkalinus (in the hyperacid cases) or hydrochloric acid solutions (in the subacid cases), then water again until the washings were clear. Then 250 c.c. of solution, one day, of potassium permanganate (starting with one to fifteen thousand and increasing to one to eight thousand and the next day a solution of silver nitrate (one to twenty thousand to one to ten thousand) was introduced into the stomach, allowed to remain there three to five minutes, and as much as possible syringed out. The patient was then given a glass of water to drink, turned on the right side and by *slow* swallowing the tube was allowed to enter the duodenum. When this was reached (in from fifteen to forty-five minutes) the duodenal contents were aspirated for study. In all these cases the duodenum was at first found to be bile-free. So far this method of treatment is no different from the procedure to be followed for the proper diagnosis of diseases of the gall-bladder and biliary ducts. The preliminary report of this method I have published.[11] As was shown in that paper we utilize, clinically, for both diagnosis and treatment, an experimental method devised by Meltzer,[12] namely, to locally douche the duodenal mucosa with magnesium sulphate solution. This by local chemical or "hormonic" action serves to relax the duodenal zone, to relax Oddis's muscle, near the ampulla of Vater, and to simultaneously (or nearly so) cause the gall-bladder to compress its walls and to expel its contents. That this is actually true is capable of a successful demonstration in nearly all cases. I have had ample opportunities to convince myself of it and those who are associated with me, and those to whom the method has been demonstrated have also become convinced.

Now to return to the application of this method in treatment. After the duodenal contents have been aspirated for study I introduce through the tube 50 to 100 c.c. of 25 per cent. saturated

[11] Lyon, B. B. Vincent: Jour. Am. Med. Assn., September 27, 1919, lxxiii, 980–82.
[12] Am. Jour. Med. Sc., April, 1917, cliii, 469.

solution of magnesium sulphate and bathe or douche the duodenal mucosa. By connecting up the duodenal tube with a vacuum bottle (low pressure), some magnesium sulphate remaining in the duodenum is first aspirated, and shortly afterward this clear solution will be seen to be tinged yellow with bile. Later nothing but pure bile is obtained. The first bile obtained must obviously come from the common bile duct, since it is the first available source of supply. As the gall-bladder contracts and expresses its contents through the cystic duct it washes out ahead of it the common duct bile and presently we get only bile from the gall-bladder, with perhaps a few drops of added liver bile; after the gall-bladder contents have all been expelled and we continue to aspirate we recover bile freshly secreted from the liver cells and emptied into the hepatic ducts, and thence to the common duct and finally (*via* the duodenum) out into the vacuum bottle; thus, as I showed in my previous paper, we can segregate for study bile from these several sources and to differentially study them, and I sketched in that paper the type of bile seen in normal and variously diseased states. Since the publication of that paper I have recovered and identified in several instances, by cytological examination of the gall-bladder bile, columnar deeply bile-stained epithelium. This more satisfactorily proves the source of the so-called "B," or gall-bladder bile. In the treatment of this second group of 7 jaundiced cases I found that in all instances the common duct, or "A" bile, was thicker and more viscid than normal; "off color," that is, deeper molasses yellow in some cases, mustard color in others, turbid and containing much mucus in ropy, tenacious masses and much flocculent debris. Microscopically there were seen the products of catarrhal inflammations, and in one case, only, micro-organisms (streptococci) were observed and later culturally proved. The gall-bladder, or "B" bile, was also found definitely "static" and off color, thicker and more viscid than normal, and several specimens contained heavy deposits of bile crystals and some microscopic catarrhal elements. No bacteria in these cases were ever found in the "B" bile specimens. In only 2 of the 7 cases was it possible to unplug the ampulla of Vater at the first treatment, but in all cases this was accomplished by the third treatment or before. Treatment should be given every day until the bile duct has first been freed and thereafter every second to fourth day, as indicated in these individual cases. Following the biliary drainage the duodenum should be disinfected with potassium permanganate or silver nitrate solutions of the same strength as used in the stomach and continued as long as the microscopic evidence of duodenitis exists. I introduce only from 100 to 200 c.c. of these solutions into the duodenum, let it remain there from three to five minutes and try then to recover what I can (often up to 50 per cent. of the amount introduced), but I have long ceased to worry about baneful effects

from that left behind, for I have seen no bad effects when $KMNO_4$ or $AgNO_3$, in the strengths up to one to ten thousand, are applied to the duodenum. Beyond this I have not tried to go, because I believe they are effective strengths. In some instances I have followed the treatment by giving a duodenal enema after the method of Jutte.

The whole description of this method of treatment and diagnosis sounds difficult and cumbersome, but it really is not so. It is true that it requires time (from one to one and a half hours), and often makes a demand on our patience as well as on our patient, but the results justify the means. And now what are the results? In the 7 cases so treated the average duration of jaundice was seventeen days and the shortest case was eleven days. Compared to the average duration of thirty-five days of the first group of patients treated by the expectant plan, this is a reduction of over 50 per cent. Not only is the duration of the disease shortened and the symptoms more promptly ameliorated, but the future dangers of damage to the biliary apparatus, from static or infected bile, from overdistended and consequently atonic gall-bladders, are to a proportional extent avoided.

I am appending a protocol of one of these cases in some detail as illustrative of the group.

Case No. XV.—W. P. A., male, aged twenty-three years. Ensign, U. S. N.

The patient had an attack of rather mild influenza on October 5, 1918 (during the epidemic). His symptoms were excessive tiredness, aching in back and leg muscles. Dull, heavy feeling in the head. Loss of appetite. Chilliness and slight fever. He had no sore-throat, but had a loose, bronchial cough, with copious purulent sputum. After several days he noticed a sense of pressure-heaviness in the epigastrium after meals, and he began to have regurgitations of food and gas odors, reminiscent of food long after he had eaten it. Several days later he noticed that his urine was becoming very dark in color.

He was first examined by me on October 11, when his chief complaint was soreness and pain in the stomach, with a sense of nausea and acute sour eructations. Gastric siphonage recovered something over 2000 c.c., sour, heavy chyme, with some food recognized as having been eaten fifteen hours earlier. Mucus, double plus. Free HCl, 7.5; total acidity, 47.5; occult blood not present.

Thorough gastric lavage given by stomach tube and Leube-Rosenheim method.

Physical Examination. Practically negative except for furred tongue, heavy breath; low blood-pressure, 104–81; enlarged area of gastric tympany after moderate air-bulb inflation and soreness over epigastrium.

October 12. Fifteen hours' fasting stomach residuum: 50 c.c., pea green, turbid, very mucoid and stringy. Free HCl, 5; total acidity, 15; occult blood, positive to benzidine, trace to guaiac. Microscopy.

Very few "food rests," starch remnants and fat globules. Much mucus. Few polymorphonuclear leukocytes, with protoplasm practically intact, considerable desquamation of endogenous epithelium; bacterial flora definitely increased; cocci and variously sized bacilli noted. Cultures planted. Fractional examination: Hyperchlorhydric curve commencing at forty-five minutes and well sustained for two and one-quarter hours, when the free HCl was 55, acidity 70 and total acidity 75. Mucus plus, no biliary regurgitation, slight motor delay. Stomach rinsed and disinfected. Tube passed into the duodenum; entered in twenty-five minutes. Duodenal contents: 9 c.c.; thick, viscid, turbid, flocculent, bile-free, with nearly 5 c.c. of granular sediment. Free HCl, 0; total acidity, 3.5; occult blood positive to B. and G. Microscopy: Mucus, plus, poorly stained necrotic debris. Many leukocytes (polymorphonuclears). Bacterial flora very noticeable; cocci and bacilli noted. Cultures planted.

October 16. Patient slightly jaundiced. Yellow scleræ and light lemon-color tint to the skin. Urine heavily bile-stained. Stool pale, pasty and fermentative. Epigastric discomfort. Gastric lavage and disinfection; mouth and nose disinfection.

October 18. Jaundice well established, of deep golden yellow. Liver dulness slightly increased. Sore to deep percussion. Stools acholic. Gastric lavage and disinfection. Duodenal disinfection with $KMNO_4$, one to ten thousand. Magnesium sulphate douche; common bile duct completely plugged and would not open. Culture made on October 12 reported: From stomach: staphylococci, streptococci, spore-bearing bacillus. From duodenum: staphylococci, streptococci, bacilli of colon group and an unindentifiable diplococcus Gram "positive, negative."

October 19. Same direct treatment of stomach and duodenum. Bile duct partially opened after magnesium sulphate, and the bile was thick, ropy, tenacious, turbid and dark mustard yellow color. Microscopically: much bile-stained epithelium enmeshed in mucus; many polymorphonuclear leukocytes, with intact protoplasm; necrotic, poorly staining debris; bile crystals; bacteria plus; bacilli and cocci; some definitely arranged in chain formation. From now on the following treatment was practised: Gastric and duodenal lavage and disinfection using potassium permanganate in increasing strengths, magnesium sulphate douche and biliary drainage on October 21, 25, 30 and November 7, and the same plan, only substituting silver nitrate disinfection, on October 23, 28, November 1 and 4.

October 25. The jaundice has completely disappeared. The urine was normal. The stools were normal. The patient's appetite has returned and he has more ambition and "punch." Duration of jaundice eleven days.

November 4. Smears from the duodenum showed: A very striking diminution in the bacterial flora; no polymorphonuclear

leukocytes were observed; no necrotic debris. Occult blood was negative.

November 8. The patient was discharged to duty.

The protocol of this patient was very little different from the others, and was selected because it illustrated the method and its results. Finally, I desire to state that this protocol was made up from the original notes and was not reconstructed from memory.

THE OCCURRENCE OF HYPOCHLORHYDRIA IN GALL-BLADDER DISEASE.[1]

By R. C. Fravel, M.D.,

ASSISTANT SURGEON, ST. LUKE'S HOSPITAL, RICHMOND, VIRGINIA.

Less than a decade ago, chronic surgical indigestion began to be recognized, the principal causes being gastric and duodenal ulcers, gall-stones and chronic appendicitis.

The train of symptoms—pain, nausea, distention, eructations, and pyrosis—is said to be due to pylorospasm and this in turn to an increase of hydrochloric acid in the stomach. The most modern authors speak of pylorospasm as the result of hyperacidity, frequently of neurotic origin, but warn that organic gastric conditions and extragastric lesions must not be overlooked. In the discussion of nervous gastropathies in *Modern Clinical Medicine*, while referring to the neurotic and dietetic indiscretions as a cause, it is stated: "Take care not to overlook gastric and duodenal ulcers or reflex causes of hyperacidity, such as cholelithiasis, chronic appendicitis and ileal stasis." The same volume under symptoms of gall-stones mentions reflex disturbance of the stomach (hyperacidity).

Kaufman, in Forchheimer's *Therapeutics*, says that hypersecretion and pylorospasm are closely interlocked, that next to gastric and duodenal ulcers, gall-stones and chronic appendicitis are the most frequent centers of irritation and causes of the irritating gastric disorder. He thinks that hyperchlorhydria is likely the cause of ulcer, gall-stones and appendicitis, the increased acid being due to some underlying condition causing irritation of the vagus nerve.

Moynihan,[2] in discussing hyperchlorhydria and ulcer says: "Hyperchlorhydria is present in other diseases, notably cholelithiasis and appendicitis, and its presence possibly explains the mimicry of the symptoms of ulcer by these various diseases."

One might continue quoting others along this line almost indefinitely, for the recent literature contains innumerable papers supporting gastric disorders in gall-bladder disease as due to hyperacidity.

[1] Read at Richmond Surgical Society, April 2, 1918.

[2] Lancet, January 6, 1912, p. 9.

I wish to present the following report of gastric findings in 61 cases of bile-tract infection, with and without stones, proved at operation, which I have had the opportunity of studying at St. Luke's Hospital. The total number of gall-bladder cases recorded is about 700, but unfortunately in the majority of instances a gastric analysis was not made. In some patients the disease was found during the course of operation for other abdominal conditions, in others the history, symptoms, and physical findings made the diagnosis clear and the patients were not subjected to the stomach-tube. In the cases reported the Ewald test-meal was used, the free and combined acids estimated by titration with one-tenth normal sodium hydroxide after the addition of Topfer's reagent and phenolphthalein. The analyses were made by a most competent pathologist, Dr. E. Guy Hopkins.

Of these 61 cases 16 show an absence of free HCl, 45 show free HCl, of less than 20, 11 come in the bounds of normal and only 5 cases show an increase of free HCl. Referring to the total acidity we find 11 cases showing a total acidity of 50 or more and 39 show a total acidity of less than 40. No cases have been included that show any associated organic stomach condition, cancer or ulcer, or malignancy of the gall-bladder or pancreas.

While the findings reported are different from previous teaching we are not alone in our observations, for there is an increasing number of articles appearing in which the authors find a low percentage of hydrochloric acid in gall-bladder disease.

Hohlweg[3] states that hypochlorhydria is an important sign of gall-bladder disease occurring in from 71 to 84 per cent. of cases.

V. Aldor[4] found in 61 per cent. of his cases either normal acidity or subacidity. His article is abstracted in *Progressive Medicine* (December, 1914), and the reviewer states that his figures are at variance with the view generally held, namely, that hyperacidity is the rule.

Olly[5] reports 87 cases of uncomplicated gall-stone disease and found that in the great majority of cases hypo-acidity is the rule.

Hernando[6] calls attention to the high percentage of cases showing gastric anacidity.

Wohl[7] reports that more than half his cases show a great diminution or absence of hydrochloric acid.

Hamburger,[8] in discussing subacidity, gives as one of its causes gall-bladder disease.

From the number of cases that we report, and from the limited evidence from other observers, compared to the vast literature that

[3] Deutsch. Arch. f. klin. Med., 1912, cviii, 255.
[4] Wien. klin. Wchnschr., 1914, No. 18.
[5] Arch. f. Verdkrank., 1915, xxi, 128.
[6] Arch. des mal. l'App. Dig., 1914, p. 274.
[7] New York Med. Jour., February 24, 1912, p. 347.
[8] Med. Clinics of Chicago, January, 1917.

Case No.	Free HCl.	Total acidity.	Operative findings.	
1	4	44	Cholecystitis.	
2	14	26	"	
3	6	20	"	
4	24	58	"	
5	6	30	"	
6	0	10	"	
7	45	65	"	
8	15	65	"	
9	10	38	"	
10	17	33	"	
11	11	26	"	
12	10	45	"	
13	8	80	"	with stones.
14	22	48	"	"
15	0	18	"	"
16	32	56	"	"
17	22	45	"	"
18	14	22	"	"
19	18	36	"	"
20	29	49	"	"
21	0	14	"	"
22	0	11	"	"
23	5	20	"	"
24	9	35	"	"
25	30	50	"	"
26	0	16	"	"
27	6	35	"	"
28	35	46	"	"
29	20	58	"	"
30	10	38	"	"
31	0	14	"	"
32	6	16	"	"
33	6	29	"	"
34	25	34	"	"
35	4	24	"	"
36	20	47	"	"
37	0	12	"	"
38	11	40	"	"
39	0	9	"	"
40	10	50	"	"
41	0	5	"	"
42	20	30	"	"
43	15	40	"	"
44	0	24	"	"
45	0	36	"	"
46	10	36	"	"
47	0	8	"	"
48	0	6	"	"
49	10	15	"	"
50	40	62	"	"
51	40	54	"	"
52	0	40	"	"
53	17	39	"	"
54	0	10	"	"
55	10	18	"	"
56	5	22	"	"
57	18	58	"	"
58	0	4	"	"
59	20	42	"	"
60	12	28	"	"
61	20	39	"	"

finds hyperacidity the rule, we do not think we have undisputed evidence, but this has been our experience, and we look for a cause of the low acid secretion as well as an explanation of the digestive symptoms.

Hypo-acidity may be the result of loss of a hormone that is secreted by the normal gall-bladder, which loss inhibits the secretion of hydrochloric acid, or it may be due to a disturbance of intermediate chloride metabolism.

There may be several factors, either separately or combined, which contribute to the gastric symptoms. Eructation, accumulation of gas, oppression, fulness after eating, pyrosis and such common digestive symptoms are as likely to be found with diminished acidity as in overproduction.

We believe with Hamburger that the pain in these conditions, as in gastric and duodenal ulcer, is due to the increased intragastric pressure. He has shown that pain occurs coincident with increased intragastric pressure in stomachs in which there is a complete absence of acids.

Pylorospasm, which has so often been the explanation of reflex gastric pain, may be the cause of increased intragastric tension and may occur in cases of subacidity.

A review of the normal action of the pylorus is necessary when one claims anything so radically different from the usual teaching. Cannon and others have shown that when food is taken into the stomach the pylorus almost immediately opens and some food passes out into the duodenum. The presence of this acid chyme in the duodenum causes closure of the pylorus, which does not open again until the acid is all neutralized by the alkaline duodenal contents. Pylorospasm is the almost continuous contraction of the pylorus, said to be and in most cases is due to increased acid secretion. But after all it is only a relative disproportion of acid to alkali, and if some day we find that in bile-tract infection there is a low alkali percentage in the duodenum, the same disproportion of acid to alkali would exist even though the acid were diminished, and pylorospasm would be the result.

Another cause for the gastric symptoms may be due to spasm caused by irritation from disease. Physiologists have shown that irritation in one part of the intestinal tract causes spasm in the region above, so the natural place for contraction spasm from gall-bladder disease would be the pylorus irrespective of the amount of acid.

One of the most frequent gastric symptoms that we have noticed is the accumulation of gas in the stomach. The oppression caused thereby and the eructation in the light of our findings is attributable to poor digestion of proteids and the consequent fermentation.

Along with this observation of hypo-acidity in gall-bladder disease would naturally arise the question of cholecystectomies as a routine procedure in all cases of gall-bladder affections. Whether

the gall-bladder has a function or not and the effect of its removal must be decided before we can dogmatically say that all diseased gall-bladders should be removed.

Hohlweg[9] made the observation which is not at all new that patients who have undergone operation for the removal of the gall-bladder not infrequently return with gastric symptoms. He had the unusual opportunity of studying 42 cases and was astonished at the hydrochloric acid deficiency in 83.3 per cent. He was able to show that a similar phenomenon could be produced in dogs after cholecystectomy.

Kemp demonstrated that there is a difference in the alkalinity of the bile before and after it enters the gall-bladder, showing that the gall-bladder must have some function.

Rost found that animals without gall-bladders secreted only one-third as much bile and pancreatic juice as animals with gall-bladders, even though normal stomach contents were injected into the duodenum. He believes this is due to the lowered production of secretin, as it could not be due to the reduction of hydrochloric acid.

Ohly, quoted by Leede in *Northwest Medicine*, found that after loss of the gall-bladder 70 to 80 per cent. of cases showed anacidity and achylia gastrica. In a series of 39 cases of this type 71 per cent. showed lack of free HCl, 17 per cent. showed free HCl below 20 and 12 per cent. were normal.

In another series of 45 cases in which stone-occlusion of the cystic duct or strong shrinkage of the gall-bladder was found, 84 per cent. showed no free HCl, and 14 per cent. were below normal.

The deductions of Leede are that any condition that brings about loss of function of the gall-bladder disturbs the secretion of the hydrochloric acid, with more or less disastrous results to the patient.

Many observers have noted the attempt on the part of the bile ducts to dilate and form, as it were, a new gall-bladder so far as the intermittent flow of bile is concerned.

The loss of a hormone is taken up by Leede. He believes that possibly a hormone is secreted by the gall-bladder which causes the secretion of HCl in the stomach, the acid chyme passing into the duodenum, causing the production of secretion, and this in turn acting on cells of the liver and pancreas, causing a production of their respective juices.

To go further into the surgery of the gall-bladder is entirely out of the province of this paper, which is primarily a report of gall-bladder cases that show gastric subacidity in the vast majority. It would seem in passing, however, that if we are anyway nearly right the proper procedure in gall-bladder surgery would be to study the function of the gall-bladder, using the acid produced in the

[9] Prog. Med., December, 1913.

stomach as an index to the remaining function of the gall-bladder and preserve all those that seem capable of functioning.

In conclusion we must remember the inaccuracy of a single stomach analysis in individual cases, also that fractional analysis is far superior, a procedure we propose to carry out in another series of gall-bladder cases. However, much importance should be placed on the high percentage of cases in such a series that show hypoacidity.

THE TREATMENT OF HYPERTENSION.

By Eli Moschcowitz, A.B., M.D.,
PATHOLOGIST TO BETH ISRAEL HOSPITAL, NEW YORK CITY.

In a previous paper[1] I discussed the relationship of hypertension to arteriosclerosis and nephritis and described a "type" individual in whom hypertension and hypertensive states are commonly found. I predicated the conception of hypertension as a primary pathological physiological state, due to unknown causes, and that arteriosclerosis and nephritis were not primary but secondary manifestations, consequent to the hypertension itself or to the cause or causes of the hypertension. In this conception, hypertensive states are subject to the same laws of circulatory dynamics as other cardiovascular disorders (*e. g.*, valvular heart disease) and have the same compensated and decompensated phases. I also tried to show that persistent hypertension represents a progressive process; that in all probability most hypertensive states begin as cases of "essential" hypertension, and that unless complicating factors are introduced such cases eventually develop the graver evidences of cardiac and renal insufficiency, affording the clinical picture of arteriosclerosis, coronary disease, chronic nephritis, etc. I also tried to emphasize the lack of relationship between the clinical and laboratory findings in hypertensive states and pathological anatomy, and attempted to show that many of the clinical phases of hypertensive states (especially nephritis) have no predictable pathological substratum, as far as "type" kidney is concerned.

The "type" individual that I have described is a combination of both physical and psychical characters. Briefly, these individuals are overweight, have short necks and are slow and unathletic in bodily movement. Psychically they may be described as prematurely old. They lack the ability to play, either mentally or physically; their imaginations are stunted, their mental range is narrow, but within its limits terribly intense. As their moments of relaxation are few they burn up their energies swiftly, until at

[1] Am. Jour. Med. Sc., November, 1919.

middle age they are exhausted, and the rest of their life is spent in seeking health. To my mind the states associated with hypertension are essentially by-products of the struggle for existence, the ultimate consequences of "the strenuous life."

With these theses in mind I shall discuss the treatment of hypertension under the following headings in the order of their importance: 1. Instruction of the Patient. 2. Reduction Diet. 3. Exercise and play. 4. Drugs.

1. Instruction of the Patient. "Blood-pressure" in the minds of most patients is synonymous with apoplexy and Bright's disease, and it is only too true that many patients on being told that they have increased blood-pressure promptly become confirmed hypochondriacs. Every trivial symptom henceforth is ascribed to the "blood-pressure" and is magnified to the nth degree. The patient becomes morbid, irritable, introspective and becomes a pitiable subject of that mental anguish termed "anxiety neurosis." Such patients would have been better off had they been told nothing.

Extreme tact is therefore necessary in imparting the status of things to the patient. The significance of the malady must be minimized to the utmost. It is important to gauge the temperament of the patient carefully and no more or less should be told than is sufficient to make the patient realize the necessity of following instructions. The best *rapprochement* between physician and patient will be obtained, I believe, by a tactful explanation of the nature and significance of hypertension. Here, as in every other relation between physician and patient, the doctor should be a teacher, as well as a healer.

The advice so lightly and so frequently given, that patients with hypertension should "retire" from business, I deem especially pernicious. The rapid aging of patients after "retirement" is altogether too common an observation not to be taken seriously. I do not know who it was who said that it is the triad—work, play and a sense of responsibility that keeps people mentally young. When these things are suddenly taken away there comes an "early and crabbed age." The advice to retire would not be so bad if an attempt were made to substitute another variety of mental occupation, but, as a rule, no such attempt is made. The consequence is that these poor souls wabble in space and have no anchorage to existence except their illness. Their main occupation thenceforth becomes the elusive quest for health.

For these reasons I advise such patients to stick to their work. In some cases it may be necessary to shorten the hours or to devolve some of the details of the business upon other shoulders. New ventures or vast expansions are prohibited. Occasionally, if the business is not entirely congenial, new lines of replacement activity are suggested, such as work in charity or social service or the culti-

vation of a hobby. Whatever activity is advised it must be something which will give pleasure. An uncongenial task is worse than none at all.

These patients must also be instructed in the very great value of holidays. Holidays are of value not only because they furnish the element of change but also because they afford opportunity to derive new mental impressions and a fresh viewpoint.

2. DIET. The diets that have been recommended for hypertensive states are numerous and various. Most of them revolve around the principle that the protein must be cut to a minimum. As far as I can see a low protein diet for hypertensive states is simply a therapeutic legacy, unfounded on any experimental or empiric evidence. A high protein diet, especially of meats, was considered bad because the split proteins resulting from digestion were supposed to injure the kidney epithelium, damage the blood-vessels, increase the albumin, and thereby bring about a quicker dissolution. I know of no evidence, either clinical or experimental, that unqualifiedly prove these things. Epstein deserves great credit in having shown experimentally and therapeutically that in one type of kidney disease characterized by large quantities of albumin and edema which he terms "parenchymatous nephritis," a high protein diet not only makes the edema disappear but often even cures the malady itself, despite the high retention of non-nitrogenous products in the blood. I have never seen that a high protein diet influences either the quantity of albumin or the hypertension in hypertensive states.

These patients, as I have said, are overweight, due to overeating, lack of exercise and often alcohol.

As the result of my observations I am convinced that the conventional tables for normal weight in proportion to height are altogether too high. As in diabetes, where Allen has shown that patients do better and show a higher tolerance when the weight is reduced to a certain limit, so in hypertension it will be found that, other things being equal, both the subjective and objective improvement will be found to be at their maximum when the patient has reached a certain weight, usually lower than that which these tables prescribe. This weight should be determined in each individual instance, and it will, as a rule, usually be found that an increase in weight, sometimes only of a few pounds, is attended by an aggravation of both the subjective and objective phenomena. In this sense it is necessary to determine a threshold, as in diabetes.

The diet that is ordered is, in many respects, similar to that of a case of diabetes of fair tolerance. The diet is simple and consists principally of fruit, coffee or tea (without sugar), meat, green vegetables, salad, cheese and a limited quantity of bread. In other respects the quantity is not limited. Indeed, there is no reason why these patients should suffer hunger. When a minimum weight is

reached a further loss may be prevented by slowly adding food of higher caloric value. Alcohol is excluded simply because a good reduction cure is impossible with it. I fully agree with Cabot that alcohol has no direct influence upon hypertension or hypertensive states.

3. EXERCISE. I feel convinced that the term "rest" is the most pernicious that can be given to patients with a compensated hypertension. The fear that exercise puts a strain on the heart, and that it increases the so-called noxious products of metabolism, I have proved to my own satisfaction to be unfounded. Rest, it is true, plays a large part in the treatment of hypertension, but only in the periods of circulatory insufficiency and under certain conditions which I shall specify. But patients with hypertension in a state of compensation, no matter what the state of disordered kidney function may be, stand exercise remarkably well. Of course the amount of exercise must be graduated, and the transition from the state of lethargy to that of heightened activity must not be too sudden. It is important that it be systematic. Exercise taken capriciously is not of much avail.

The ideal form of exercise for patients with hypertension is golf. The advantages are many: (*a*) It is the least strenuous of outdoor sports. (*b*) It involves a large amount of walking without seeming effort. (*c*) It is a play and not a task. (*d*) It generates a sporting instinct, which is reflected in their mental attitude to the problems of life.

If for various reasons a sport cannot be undertaken, walking provides an excellent means of exercise. No specified number of miles is ordered; the patient is told to walk until he is tired; this varies from three to five miles a day. It should be brisk, uninterrupted and done daily. It is remarkable to see how much further a patient can walk than he formerly felt himself capable.

If for one reason or another even walking is not possible, systematic brisk massage will serve up to a certain point as a tolerable substitute for exercise.

The effect of exercise in hypertensive states furnishes another analogy to diabetes. As Allen has shown that exercise increased the tolerance of diabetics, so in hypertension the tolerance, in terms of efficiency, is increased.

The attainment of the minimum weight alone, by diet and exercise, has a truly remarkable effect in cases of compensated hypertension. Their wind is better; their aches disappear; their cardiac reserve increases; they no longer are perpetually tired; their movements are quicker; they sleep better; they are livelier mentally; in a word they become more efficient individuals. Objectively the pulse is slower; slight irregularities, probably due to extrasystoles, disappear. The effect on the blood-pressure is peculiar. The systolic pressure is lowered, but not nearly to the

extent of the diastolic, so that the pulse-pressure is increased, sometimes quite markedly.

There is nothing more hazardous than to try to judge the condition of the patient by the amount of decrease of the systolic pressure; the patient's improvement may be decided, although the systolic pressure remains where it was or is only slightly decreased. A more accurate measure of improvement is in the decrease in diastolic pressure and consequent rise in pulse-pressure. Subjective improvement more nearly goes hand in hand with a decrease in diastolic pressure and a rise in pulse-pressure, and this nearly always is accompanied by a slowing of the pulse. The significance of the slowing of the pulse will be discussed under the heading of "drug treatment." As Goepp correctly observes, it is the ratio and not the height of the pressure that determines prognosis and connotes improvement.

The improvement in circulatory pressures is accompanied by greater diuresis and diminution or even disappearance of the albumin.

Possibility of Cure. There is no doubt in my experience that the earlier the patient is seen the nearer to normal the patient can be brought by simple reduction cures. And here I venture to set forth an observation of profound importance: It has often been questioned whether a patient with persistent hypertension can ever be brought back to normal. Most authorities deny that this is possible. But I have met with perhaps a dozen or more instances in which I believe a complete cure has been effected. I mean by that that the blood-pressure has receded to normal limits; the urine has been completely freed from albumin and casts, the heart action is normal and all subjective phenomena, such as dyspnea on exertion, headaches, vertigo, palpitation, have completely disappeared. It is possible that in subsequent years something may yet develop, but thus far the patients are, for all practical purposes, well. All the patients, so far as I can recall, were early cases. The pressures were not high: the systolic varied between 150 Hg. and 170 Hg.; the diastolic was only slightly over 100; the urine showed only a faint trace of albumin and the pulse was not much increased in frequency. The amount of overweight seemed to have had no bearing. I recall one patient who was almost obese.

Rest. As I have said, rest plays an important part in the treatment of hypertension. It has three indications: (*a*) In severe circulatory insufficiencies as revealed by a rapid and irregular heart, hypostatic congestions, oligurias, with marked increase in albumin, edema of the lungs, uremias, dropsy, cerebral manifestations, etc. Here the indications are precisely those of decompensated valvular lesions. (*b*) In cases of so-called "essential" hypertension, with high systolic and diastolic pressures, a full bounding pulse and accompanied by signs of premonitory cerebral hemorrhage. It is remarkable that the brain seems to be a *locus minoris resistentiæ*,

even when the heart and kidney show no pronounced aggravation of signs. (*c*) In cases of long-standing hypertension, with marked aggravations of all the focal organic signs, with severe dyspnea and general enfeeblement. In these patients, of necessity, the enforcement of an active life would be cruel. Such patients also, I have found, gladly take to the idea of spending one entire day of every week in bed.

4. Drug Treatment. The main desideratum in the treatment of hypertension is, as I have shown, the maintenance of the best possible circulatory function; in other words, to try, if possible, to place the circulatory function in the condition of so-called "compensation." Attempts to reduce the blood-pressure by direct methods long ago have been proved futile. We have drugs that reduce blood-pressure, but their effect is evanescent and no permanent gain is ever derived. With the aid of the therapeutic means I have described, either alone or with the aid of drugs, we do effect lasting decreases in blood-pressure, but these are entirely secondary. It is entirely possible to bring about vast subjective and objective improvement without appreciable effects upon the blood-pressure, nor is this improvement, as I have shown, always proportional to the decreases in pressure. As in valvular and muscular defects of the heart the main drug upon which we rely to maintain a correct circulatory balance is *digitalis*. For many years digitalis was contraindicated in hypertension, because it was supposed to increase blood-pressure, by increasing the power of the muscle and contracting the peripheral bloodvessels. It was therefore considered *the* heart stimulant *par excellence*. We know that digitalis in the normal heart at all events never directly increases the blood-pressure, except in doses that are far beyond the therapeutic maximum. In recent years the opinion is gaining ground that the main effect of digitalis is expended in affecting the rhythm of the heart. It affects irregular hearts more than the regular; it makes irregular hearts regular and it slows regular hearts to a limited extent. In irregular hearts, as in auricular fibrillation, digitalis, it is true, increases the blood-pressure, but the effect is entirely secondary and conditional upon the improvement in the rhythm. It would lead me too far to discuss the therapeutic indications of digitalis in general, but I may say that my conception of digitalis is that of a regulator and not that of a "stimulant." It may be aptly likened to the timer of an automobile engine.

With the clearer understanding of the effects of digitalis our timidity as regards its employment in hypertension has completely disappeared. Its indications in decompensated states of hypertension with the signs and symptoms which I have outlined already are obvious. In such instances the heart is rapid and usually irregular and the effect, except in cases where the decompensation has gone too far and the reserve force of the heart has been lost,

is almost magical. These patients are the so-called "cardio-nephritides." When all signs of decompensation have disappeared, the principle consists in keeping the heart at a certain rate by the continuous use of digitalis. Each patient must be studied with this end in view, and eventually a rate will be found in which the patient's condition both subjectively and objectively, will be at its best.

But the value of and the indications for digitalis in compensated cases of hypertension have not been generally appreciated. This is a subject worthy of extensive study. I know of the therapeutic benefits that may be obtained, but I am not at all clear as to what physiological forces or agencies these benefits may be ascribed. I can best describe what I mean by citing a concrete example. A patient complains of slight shortness of breath on exertion, pains (very often anginoid) about the precordium and headache or vertigo. An increased blood-pressure is found, a pulse only moderately rapid, between 80 and 90, and perfectly regular; the urine is lessened in amount and contains albumin and casts. Place this patient upon full doses of digitalis and the symptoms disappear, the quantity of urine increases and the albumin decreases; the systolic pressure decreases only a few points, the diastolic pressure a little more. The pulse-rate at rest, however, comes down a varying number of points, from only 4 or 6 to perhaps 10 or 20, depending on the original rate. Now comes the interesting fact: if such a patient is kept at this rate of heart action he will remain well and all the other objective signs, such as the blood-pressure and the condition of the urine, will be found to remain constant. When the pulse at rest remains persistently above this rate the patient will invariably be found to be worse. This rate may be as low as 60 or as high as 90. Individualization of dosage is therefore a paramount necessity.

Why digitalis causes such pronounced improvement I am at a loss to explain. Whether the effect is entirely due to the slowing of the heart, enabling the organ to accumulate a greater reserve force in diastole; whether it increases the velocity of volume flow or whether it improves the coronary circulation, I do not know. But the fact that digitalis is a "real drug" in the treatment of apparently compensated cases of hypertension, as well as those that are decompensated, is to my mind an incontrovertible fact. Its administration requires judicious study and furnishes an abundant field for clinical and experimental investigation.

Digitalis is, of course, useless in cases of hypertension, with a constantly slow pulse (around 60). But a pulse of 74 or 80 need not be considered a contra-indication for its use.

Nitrites. The drugs of the nitrite group introduced by Lauder Brunton unquestionably diminish blood-pressure, but the effect is transient. These drugs have, nevertheless, a definite field of usefulness, but only, I believe, as symptomatic remedies. They unques-

tionably relieve what have been termed "spasm" phenomena, such as anginoid attacks, transient aphasias, numbness and paretic symptoms due to cortical irritation, headaches and vertigo. I think most of us have seen patients in whom nitrites, when first administered, cause a temporary increase in headaches. I believe it is a mistake to stop the drug for this reason because I have found that if persisted in the headaches will disappear. If nitrites are given the dose must be given frequently rather than, as usually done, three or four times daily.

Iodides. The use of iodides in hypertension was based upon the theory that arteriosclerosis caused hypertension and that the iodide compounds softened the sclerotic vessels and so reduced the tension. Inasmuch as the testimony is overwhelmingly in favor of arteriosclerosis being secondary to the hypertension, and that, furthermore, the iodides cause no appreciable softening of the blood-vessels except perhaps in syphilitic instances, this theory, therefore, lacks support. The advocates of iodide therapy cling to the more recently promulgated theory that these drugs do good because they change the osmotic tension of the blood. But I have found no evidence that they do. At all events in frank hypertensive states I have never been able to convince myself that I have accomplished anything and have therefore practically abandoned their use. The only occasions in which I still employ them are in patients with hypertension with an old history of syphilis and who complain of persistent headache. In such instances it acts better than any other therapeutic measure.

Chloral Hydrate. Small doses of chloral hydrate repeated over a long time do unquestionably reduce the blood-pressure, but I believe chloral produces this effect by its sedative action alone, just as morphin will. Patients with hypertension are liable to be "nervous" and are poor sleepers, and I question, therefore, whether chloral acts better in such cases than any of the milder sedatives and hypnotics. My observations lead me to believe that patients with hypertension need their full quota of sleep.

Caffein. The view is now generally held that the various caffein salts are pure diuretics and that their effects on the heart are practically negligible. These caffein salts do improve conditions associated with hypertension only in so far as they lessen the embarrassment of the heart by lessening the fluid content of the body. These salts are therefore eminently useful in the decompensated states of hypertension.

THE MEDICAL TREATMENT OF AORTIC ANEURYSM.

By W. W. G. Maclachlan, M.D.,
ASSISTANT PROFESSOR OF MEDICINE, UNIVERSITY OF PITTSBURGH.

The purpose of this article is to emphasize the necessity and value of medical treatment in a condition which too often is regarded as hopeless from the point of view of therapy. The aneurysms under discussion are of the thoracic aorta, and have as their etiological background the disease syphilis. One does not, however, wish to convey the impression that syphilis is the only cause of aortic aneurysm. We have in the pathological museum at the medical school two really beautiful specimens of mycotic aneurysm of the ascending aorta of known Streptococcus salivarius etiology. These have been reported by Klotz, but this is the exception while syphilis is the rule. The relation of syphilis to thoracic aneurysm has been so clearly shown by clinical, serological and pathological workers that one is not surprised at finding the two conditions, in fact, really one disease, together in almost 90 per cent. of the reported cases. We do not refer in this article to aneurysms in which this relationship cannot be demonstrated.

It is advantageous to recall, briefly, the lesion produced in the wall of the aorta by the Spirocheta pallida. The nature of the process is well established, and in practically all of the text-books of pathology it is minutely described. We would, however, refer the reader to Longcope's article, which discusses this subject in a very complete way. Syphilis produces in the wall of the aorta a granulomatous inflammation extending from the adventitia into the media and intima. The perivascular channels about the vasa vasorum of the outer two coats appear to be the road along which the spirochete passes, and it is well to keep in mind that this organism has been found in all of the layers of the aorta. Hence the presence of granulomatous tissue in any portion of the wall is to be expected. The media and adventitia show the greatest inflammatory reaction. The destruction of the media, composed as it is chiefly of elastic fibers, is considerable, the amount depending on the severity of the process. This naturally leads to weakening of the wall, and nature attempts repair by laying down fibrous tissue, the contraction of which in part gives a peculiar characteristic wrinkling to the intima, which is so valuable a sign in the gross diagnosis of syphilitic aortitis. The adventitial reaction is of the same type, but here one sees more connective-tissue change and more marked perivascular infiltration of lymphoid and plasma cells. Patchy intimal thickening is very evident.

Further, and of considerable importance, is the variable amount of gummy necrosis in the wall. From a pathological point of view

there is really no difference, save one of degree, in the inflammatory process of a syphilitic aortitis, with or without aneurysm. We have never seen an aneurysm which came to autopsy that did not show evidence of gummy necrosis in its wall, at times seen only microscopically, but often apparent in the gross. In this connection the report of Winternitz is of considerable value. He was able to observe the development of a very early aneurysm in a young syphilitic negro woman dying from coronary thrombosis. He could follow the granulomatous inflammation from the adventitia inward through the media, which was locally destroyed, and see a pouching of the intima into this area. This case, Winternitz, believes confirms Benda's view that the development of aneurysm is secondary to inflammation and necrosis of the wall and not a gradual stretching of the fibrous tissue, which replaced these necrotic areas in the process of repair or healing. We agree with this view. Aneurysm, as we are using the term, really means a chronic progressive and active syphilis of the aortic wall, hence our therapy must be in accord with this picture if we are to expect good results. That is only logical.

That the fibrous tissue areas representing healed lesions seen in the wall of a syphilitic aorta or an aneurysm lying between the ruptured elastic tissue fibers stretch under the constant pressure is most likely, but we do not feel that this plays a part of any importance in the actual production of the lesion; further, it seems to us as most improbable that the rupture of an aneurysm is ever due to the breaking or giving way of this fibrous tissue. In this connection we wish to refer to the work of one of our colleagues, Dr. C. C. Guthrie. The dog on which he did his first arterial transplantation, eleven years ago, died this past winter from a malignant tumor, with general metastasis. The transplant in the carotid was, of course, the point of interest. This was represented by a dilatation about the size and shape of a large hickory nut. This dilatation Dr. Guthrie had observed several months after the original operation, so he could definitely say that it had been present for at least ten and a half years. The wall of the dilated portion shows fibrous tissue plus the calcified remains of the transplant, with no ingrowth of muscle or elastic tissue from the adjacent carotid artery and no cellular inflammatory reaction. Here we have an example of a fibrous-tissue wall of an artery, with nothing to indicate that rupture was even impending, functioning for over ten years and in gross structure a true aneurysmal sac. The point brought out by Guthrie's experiment, which is to us of value in the localized sense of our present discussion, is that fibrous tissue can act as a vessel wall and not rupture for a period of many years, in this case lasting the lease of life of the animal. It is very probable, however, if an inflammation of any type had developed in the wall of this sac the result would have been a ruptured aneurysm. This experiment

also shows, as indicated above, that fibrous tissue may be stretched in a vessel wall to assume a sac-like appearance, but the conditions underlying the change here are entirely different from those met with in the human aorta. In man the cardinal point is an active inflammation. If we could succeed in stopping entirely this inflammatory reaction and produce healing by fibrous tissue replacement, which we know occurs then, it would be possible, by analogy, to compare this very interesting animal work with our clinical problem, particularly in reference to the prognosis.

It would seem therefore rational that the therapy of aneurysm should be directed primarily against the spirochete with the idea of its destruction, which would be followed by the eventual absorption of the inflammatory process in the wall of the vessel and the subsequent replacement fibrosis or healing. The results would depend a great deal upon the amount of damage done and how thoroughly we are able to sterilize the areas infected by the spirochete. Assuming that this latter condition is a possibility, does it not suggest a more favorable outlook for these cases? The fact that an occasional spontaneously healed aneurysm is met with, certainly seems to indicate that an enlarged thoracic aorta, if quiescent, is compatible with life. From some limited observations on aortic aneurysm during the past three years we feel that the condition is by no means as hopeless as is ordinarily considered.

The prognosis of this lesion has always been very poor. It is well known that a certain number heal spontaneously. They are met with occasionally at autopsy. On the whole, however, this fortunate group is not very large and there are probably very few physicians who have clinically diagnosed aneurysm and who have seen a so-called spontaneous cure on the same patient. Osler gives almost a hopeless outlook, but calls attention to the fact that some even unusually large aneurysms have been known to last for many years. These, he says, are not common. Of the majority, after the diagnosis has been made, a period of one or two years usually sees the end. Excepting the unusual case one would be correct in saying that thoracic aneurysm is a fatal condition in a relatively short period of time after symptoms develop. This is the consensus of opinion as given in the modern text-books and other literature.

The commonest cause of death is rupture of the sac. This rupture, we believe, is due to the giving way of the necrotic and inflammatory tissue in the wall of the sac and not the breaking or tearing of fibrous tissue which represents healed portions of the wall. Fifty-three per cent. of the 1829 cases referred to by Arnold died of rupture. Cardiac failure from myocardial and aortic valve disease, angina pectoris, asphyxia, edema of lung, hypostatic pneumonia, tuberculosis or other intercurrent infections make up the rest of the list. Even if the death is not due to rupture of the sac most of the other causes are more or less directly dependent on this

large mediastinal mass. The aneurysm itself is therefore directly or indirectly responsible for the great majority of the deaths from this condition.

The medical treatment of aneurysm, as judged by past clinical experience, has not been brilliant in its results. There is always a fatalistic touch to what is written on this part of the subject. At the best the most one appears to be able to do is to relieve untoward symptoms temporarily, particularly if the lesion is at all advanced. Most authors speak of the use of mercury in those cases in which the luetic infection is known to be of a relatively recent date or where the aneurysm is supposedly small. The use of mercury, however, is not emphasized but rather gives one the impression of being suggested *en passant*. Certainly it is not brought out with the same force that one indicates when referring to tertiary lues of almost any other source. Potassium iodide, on the other hand, has been the drug of this condition for many years. It is astounding to note how often this drug alone is given in aneurysm, when with any other tertiary luetic lesion the solitary use of iodide would be considered an inexcusable error, as it is the general belief that potassium iodide, although having great power in stimulating absorption of the syphilitic process, does not kill the Spirocheta pallida and hence does not reach the cause of the disease. We cannot help but feel that in the treatment of aneurysm not enough attention has been focussed on the inflammatory lesion in the wall of the aorta. It is here that the cause is to be met, and it does seem rather futile to hope for results if we do not try to render the aortic wall free from the infection. As far as we know mercury and arsphenamin preparations are the only ones capable of destroying the spirochete. The cardinal principle then in the treatment in which we are striving for a possible cure in the early cases or for palliative effects in the late is to deal with the process as a syphilitic one and to apply, as fervently as possible, antisyphilitic remedies. Let us attempt to heal the inflammatory lesion in the wall and trust to the patient to fill up the sac with a fibrin clot. There are several points to be observed in the treatment which it would be well to briefly enumerate.

1. Rest. As soon as the diagnosis is made the patient should be put to bed and kept there for as close to three months as possible. We allow them to get up to go to the toilet. As has been pointed out by Osler, many aneurysms will become symptomless on this rest alone. It is of the greatest value, and any treatment that does not take into account a prolonged rest in bed is falling far short of the ideal. Following the period of almost absolute rest, for the remainder of the year the patient should be limited in his physical work. We do not consider it wise to eliminate all activity, for, as a matter of fact, very few people are financially or mentally able to withstand a year of complete idleness. Undue exertion, worry and extra mental effort are to be avoided and this should more or less

be the basis for the remainder of the patient's life. It has been our experience, however, to deal with patients that were unable to take more than six weeks' rest, and following this go back to their former occupations. A change of occupation to something less strenuous is always advisable. We believe it is a good thing in many ways to have the individual kept moderately busy, as this is the best way to eliminate worry.

2. DIET. The old treatment was more or less based on diet and rest. Valsalva rested, starved and bled the patients. It must have been a very rigorous case which survived, and probably the remark that the cure was as bad as the disease was more or less true. This form of treatment was supposed to put the patient in so low a condition that the blood-pressure on the aneurysm would be greatly reduced, also possibly the coagulation or fibrin formation in the sac would be increased. The first part undoubtedly was attained. Osler recommends bleeding as an emergency measure, particularly for some severe cases of dyspnea. We have seen one case given considerable relief by this procedure. Bleeding was a very important part of the Valsalva treatment, but now it is only used as an emergency method for relief. Futcher has shown that there is no evidence to indicate the value of gelatin as a measure to stimulate coagulation in the aneurysmal sac. We do not use the calcium salts either for this purpose. Tufnell's diet is of more recent date. The patient was rested in bed and given a very reduced fare, consisting of 8 ounces of fluid and 10 ounces of solids per diem. This also is very severe. Lowering of blood-pressure, inducing fibrin formation and the benefit of rest, were the claims made for this diet. The rest is of undoubted value, but the supposed increased coagulation of the blood brought about by this method has been disproved by A. E. Taylor on two cases studied some years ago. Clinically the method is more or less discarded. We believe in moderation in this matter. If the case has a fairly high blood-pressure then a light diet is indicated. At the same time we feel that the general nourishment of the patient is to be kept as close to normal as possible. In some of our cases the diet and fluid intake were moderately limited, but in others no change was made. Our impression is that the diet is of minor importance and we can see no advantage in having the patient undernourished.

3. ANTILUETIC TREATMENT. Potassium iodide in moderate doses (gr. xv three times a day) is the drug method of treatment used for many years. The dosage may vary considerably, but the above quantity usually is sufficient for most cases. It undoubtedly has great value, as the severe thoracic pain generally is readily controlled. The ability of potassium iodide to hasten the absorption of luetic inflammatory tissue is to be kept in mind. But, as far as we know the Spirocheta pallida is not affected by this drug, hence we cannot hope to stop the inflammatory process in the wall

of the aneurysm by its use alone. As in tertiary syphilis elsewhere, mercury and arsphenamin must be added. Mercury in some form should be given and kept up for the same period as we would demand in syphilis. We have no special preference for the way mercury is to be applied. While under our care in the hospital the daily inunctions were used, but when the patient went home a form taken by mouth was substituted. Gray powder was often the choice.

Arsphenamin (diarsenol) in our hands has been quite safe and of great value. Longcope strongly recommends it in his work. We have given many injections in aneurysms and have never seen any ill results. The doses should always be small and repeated at weekly intervals. We recommend that the patient receives at least 12 injections, each of the first six being 0.2 gm. and the remainder 0.3 gm. We never give a larger dose, as we desire the patient to be free from any straining as would occur in vomiting. The arsphenamin is given while the patient is resting in bed, hence the value of making the primary rest as long as possible. In one case we gave fifteen injections. We have no definite rule, save the general condition of the patient and the Wassermann reaction to know when to discontinue the therapy. This is a very difficult problem to decide in aneurysm or in any form of syphilis. It is our intention to treat all cases actively for at least two or three years if this is feasible. We lay great importance to the frequently repeated small injections of arsphenamin at the onset during the period of rest. This is really all we have to offer, namely, treat aneurysms intensively by antiluetic measures. There is, of course, nothing new in the method, but, taking the disease as a whole, one would be surprised, we believe, to know how few aneurysms ever receive mercury or arsphenamin. From our experience there is no contra-indication to the use of the latter drug. We have given it, with very gratifying results, in a case in which the aneurysm was of enormous size, bulging through the chest wall. The solution given was never more than 100 c.c., and always diluted at least in the proportion of 0.1 gr. for every 25 c.c. of distilled water.

The following is a brief report of the salient points of our cases. From this very small list and the short duration under treatment it would be unwise and further incorrect to be too sanguine as to the ultimate value of the therapy, but there are some points which have been so different from our past experience that we feel justified in continuing this method and in presenting these facts:

We have had seven cases to observe in a period of three years, four of these are unsatisfactory from the point of record in that we have lost track of them since leaving the hospital. They seemingly did not wish to coöperate even while in our care. They were given four injections of arsphenamin (0.2 gm.) each during the month spent in the hospital in addition to the mercurials and iodide, but

at the end of this time they departed against advice. Subjectively they were free from symptoms, and this is probably why we were not able to hold them further. Despite promises to return for observation they have been entirely lost sight of. It would be very unwise to say anything further on this group, except that they took the antiluetic treatment well and improved with one month's rest. Two of these aneurysms had all the physical signs of being large and well advanced.

Of the other three we have more complete records. They are under our observation from time to time.

Case I.—O. K., aged thirty-six years, molder, primary lesion fifteen years before onset of symptoms, enjoyed excellent health until July, 1916, when he suddenly developed attacks of dyspnea of a paroxysmal type, accompanied by substernal pain. He was sent by his physician to Dr. B. M. Dickinson for a nose and throat examination. This was negative, and he was referred to the medical service of Dr. J. A. Lichty in August, 1916, or six weeks after his first symptoms. The physical examination showed a very apparent pulsation in the first and second interspaces on the right and in the episternal notch, with a distinct lifting of the sternal end of the right clavicle with each pulsation. An expansible character was noted by palpation. There was increased dulness to the right of the sternum above the level of the upper border of the third rib. The heart sounds had the peculiar quality heard in dilated aorta and further showed a systolic bruit. The auscultatory signs were most evident just under the clavicle. Roentgen rays showed an enlargement of the ascending aorta, with a sacular-like bulging where it curved into the arch. The arch was but moderately involved in the dilatation while the descending thoracic aorta appeared normal. By fluoroscopy an expansile pulsation in the aortic bulging was clearly seen. The Wassermann reaction was positive. The heart appeared normal, as did the rest of the systems. There could be no doubt of the diagnosis of aneurysm of the ascending and of the arch of the aorta.

The patient was eager to get well and remained in bed six weeks. He was given a general diet and allowed to go to the toilet. Potassium iodide, gr. xv, three times a day, ℥j of ung. hydrargyrum rubbed into the skin daily, and 0.2 gm. arsphenamin once a week for six weeks was the therapeutic procedure while he was in the hospital. He showed no untoward symptoms after the intravenous injections. He had two attacks of dyspnea during the first week in the hospital, but after this he was free from symptoms and confessed to feeling perfectly well. On his discharge, as he was an intelligent fellow, we instructed him to keep up the iodide and the mercury inunctions which he has followed, we believe, faithfully for three years. The dose of the iodide was, however, diminished, as lately he has become somewhat intolerant to its use. He returned

weekly to the hospital for one month after discharge and four doses, 0.3 gm., arsphenamin were given. In January, 1917, he had three more injections of 0.3 gm. arsphenamin. This was the final number. We have now taken him off mercury after a three years'

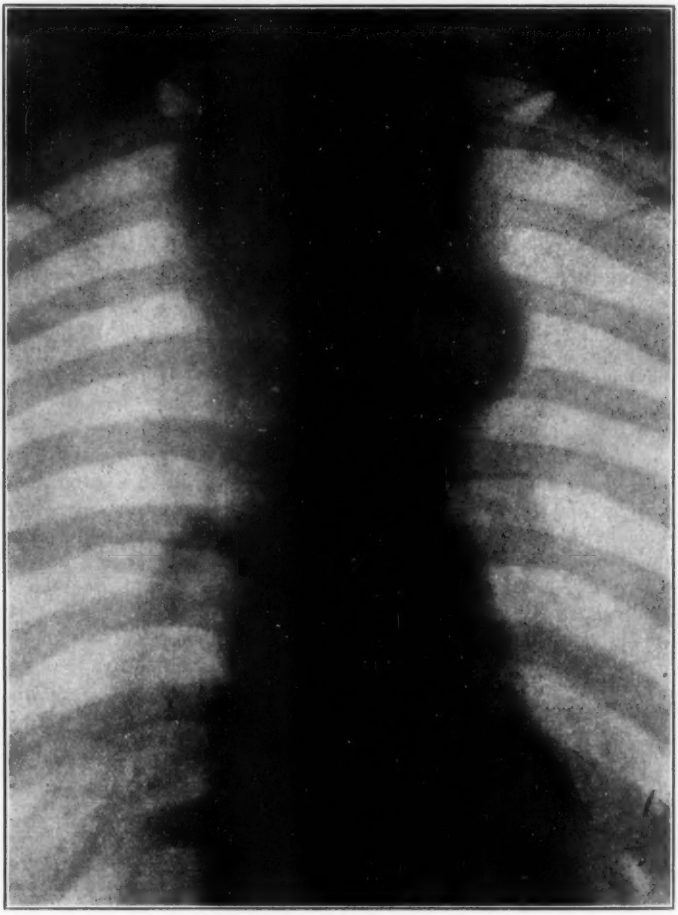

FIG. 1.—Case I. Plate taken shortly after admission to hospital in July, 1916.

course. A rapid review for the past three years has some points of interest: He has been apparently perfectly well and has worked almost every day since leaving the hospital. We cautioned him against working too hard, but to no avail. Before leaving the hospital our intern, with most characteristic teutonic diplomacy,

told him frankly that his case was hopeless and some day he was going to choke to death. This remark we know has never entirely left his mind and accounts for his subsequent, almost foolhardy actions in working. In July, 1917, one year after the onset, he was in apparent perfect health, the Wassermann was negative, but we could get typical physical signs of an aortitis or a dilated aorta,

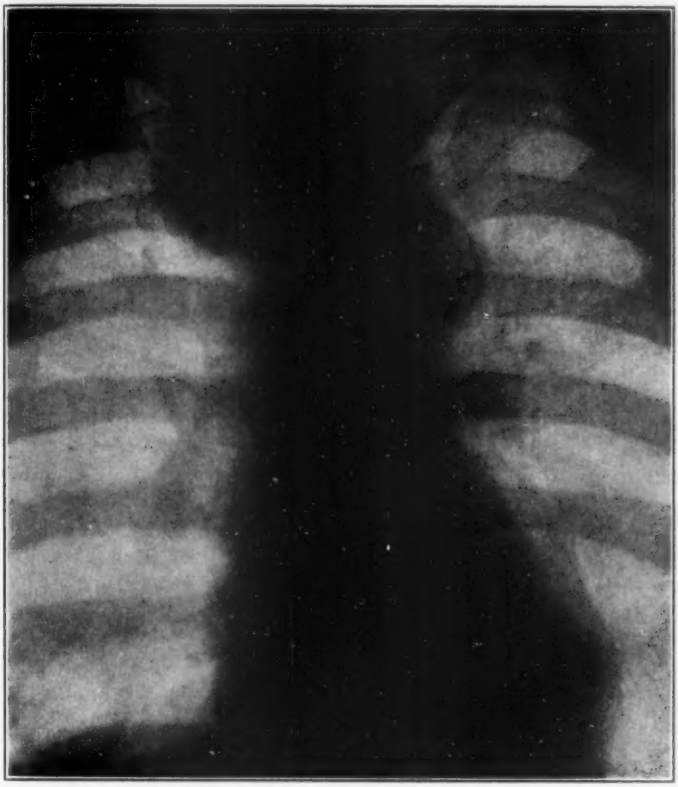

FIG. 2.—Case I. Plate taken three years after in September, 1919. Note the line of calcium deposit in the wall of the sac.

and the roentgen rays showed almost the same picture as it did the previous year. He was able at this time to pass a fairly close physical examination into a large manufacturing concern, where he made shells for eight months. This work entailed the lifting of 130 pounds (the shell weight) between 100 and 120 times a day, certainly the last thing in the world for a man with an aneurysm to attempt. The reason for this was an economic one: shell-making

was a remunerative job, and he desired to leave as much as possible to his family, firmly believing that the ill-advised remark of the house man might come true any day.

He, however, appeared to be none the worse for this physical test, but was willing to get much lighter work, which he has been doing up to the present. Even the present work, in charge of the repair shop of a garage, gives him very long hours and is relatively hard. Six months ago he fell off a ladder and broke the seventh rib in the anterior axillary line. At that time he noticed very carefully for any sign of pain or discomfort over the aortic area, but none was present. Today he feels perfectly well, looks outwardly in good health, shows signs of slight aortic dilatation, which we would call an aortitis if this were the first examination. His Wassermann is negative. The roentgen rays indicate that he still has his dilated aorta, or aneurysm, with some calcification in the sac wall. There is no expansile pulsation to be palpated, and there is very little evident expansion under the fluoroscope. We do not believe the sac has enlarged.

This type of aneurysm, of course, is the favorable one, and we probably saw it fairly early, although he must have had his aortitis for a considerable time. We trust the sac is filled with organized clot, but we do hope there are no living spirochetes in the wall of the aorta or elsewhere. We are under the impression that if fibrous tissue has replaced all the damage done to the coats of the aorta that this reparative process will, from the point of view of function, carry on for some years.

Case II.—P. G., aged thirty-five years, laborer, came to the hospital July, 1918, with a pulsating mass protruding in the second right interspace immediately to the right of the sternal border. He complained of some coughing and pain of a sharp, cutting character, usually noticed at night in the chest under the sternum; he could only sleep sitting up in bed or in a chair, could not lie on his side nor could he bend over, and he was forced to stop work on account of the pain produced on using his arms. He is an Italian, and during his stay at the hospital was most difficult to handle. The diagnosis was so evident that we are only mentioning one or two points. The pulsating expansile mass on the right side of the upper chest protruded between the second and third ribs. It was round at the base, having a diameter of 4 cm., the ribs being pushed apart, and it extended outward 2 cm. from the chest wall. The surface had a gentle curve, with a tendency to taper toward the outermost portion. A very marked enlargement of the aorta, by percussion, was easily demonstrated on both sides of the sternum, and the roentgen-ray plate showed the aortic shadow to be as large as the heart. The ascending aorta, arch and part of the descending thoracic aorta was involved. The fluoroscope showed it to be a pulsating expansile mass. Undoubtedly the aneurysm was a very

large one. The Wassermann was positive. The primary lesion was denied. There was a slight regurgitant aortic lesion, but not a great amount of cardiac hypertrophy was present, and the heart's action was regular and of good quality.

FIG. 3.—Case II. Plate taken at the time of admission. (The roentgen-ray plate made fifteen months afterward showed a shadow similar to the above, but unfortunately it was not clear enough to reproduce, and we have been unable to get the patient to return for another.)

We were very unwilling to try arsphenamin, and, in fact, kept him under observation for two weeks before giving the first injection; but we concluded that from the man's point of view it was worth the risk. It was the size of the aneurysm that made us hesitate. He took the arsphenamin perfectly and was given ten 0.2 gm., and four 0.3 gm., in all over a period of fourteen weeks. Potassium iodide, gr. xv, three times a day, and a daily inunction of mercury

were given while in the hospital, a period of sixteen weeks. These last two preparations had been used from the first. After leaving the hospital we gave him gray powder and iodide, as we felt sure he would not apply the ointment. We now know definitely he has not taken any medicine since leaving us. It was practically impossible to get him to stay in bed, and only on account of his interesting lesion did we tolerate his disobedience. After two months the aneurysmal sac protruding from the chest wall showed signs of decreasing in size, and at the end of sixteen weeks it had entirely disappeared, the chest wall anteriorly resuming a normal contour. The second and third ribs had a normal relationship, although we could distinguish on palpation some irregular thickening along the free margins. In the interspace one could readily get the pulsating sac with the tip of the finger. This disappearance of an aneurysm from the surface is known to occur, and it sometimes happens at the expense of growth of the sac elsewhere. We had no indication, however, of this occurring. The patient during the last month seemed to appreciate he was improving, and we were able to get him to rest in bed for a few hours during the day. His symptoms, save for an occasional brassy cough, disappeared, and he left the hospital feeling well and intending to go back to work at once on a light job. His Wassermann reaction at the end of his hospital stay showed a negative fixation with the lipoid, but definite positive with the cholesterin antigen. The roentgen-ray picture gave a shadow of about the same size as at the onset. He was on a general diet. After leaving the hospital, which he did on account of the inrush of influenza patients, we heard of him only indirectly. It was impossible to get him to report, and only through the kindness of one of the officials of the steel company where he was employed were we able to get in touch with him. After fifteen months he made his first appearance, and he really looked very well. He has been working steadily since leaving the hospital, and his work has not been at all times, by any means, what we would call light or easy. The physical signs are just what they were when he left. The roentgen rays and fluoroscope show that the sac has not changed any in that time. He stopped taking mercury and potassium iodide the day he left the hospital, as we imagined he would. The Wassermann reaction now is strongly positive with both antigens. We gave him some good, sound advice, put him back on mercury and iodide and commenced another series of arsphenamin injection, but after two weeks he again disappeared, and in all probability will not return until he develops more symptoms. Unfortunately, however, we are losing or have lost the good start we made last year in this case. It is too bad that this patient is so refractory, because if one could get some results with an aneurysm of this size under difficulties then we should be able to do a great deal more when conditions are more favorable. This aneurysm is undoubtedly very large, and

when we consider that over a year ago he was not able to sleep except sitting up, could not bend over or lie on his side, and had a very harassing cough, with a good deal of thoracic pain, we must conclude that from the point of general well-being he is clearly improved. This we would hardly expect without treatment after fifteen months in an aneurysm of this size. It is further very unfortunate he did not take the mercury as directed during the past year.

CASE III.—W. R., aged forty-two years, was admitted to Dr. J. A. Lichty's service in August, 1918, suffering from nocturnal dyspnea and severe, almost constant, deep thoracic pain, which at times was cutting in severity. These symptoms appeared in January, 1918, but for the year before that he had been in rather poor health, although not suffering especially from the chest symptoms. A very large aneurysm, involving the greater part of the thoracic aorta, was readily apparent on physical examination. A diffuse throbbing pulsation of the whole upper chest and vessels of the neck, dulness on both sides of the sternum above the cardiac area, particularly on the left side, tracheal tug, systolic murmur over dull area, expansile enlargement almost of the heart size by fluoroscopic examination and roentgen-ray plate, typical of a large thoracic aneurysm, chiefly of the arch and first part of the descending aorta, could be made out. The Wassermann was strongly positive. There was a regurgitant lesion at the aortic valve and some left-sided cardiac enlargement. Compensation appeared to be good. An indefinite primary lesion was present twenty years ago. He remained in bed for the month of August. He unfortunately could not rest for a longer time, as it was practically impossible for him to get away from his business. He was virtually alone for one continuous year without a day off, after his rest in the hospital managing a busy retail hardware store in one of the very active towns of this district, and to make matters worse, the influenza epidemic carried off his head clerk, so that for this patient mental and physical rest, which is so important, was not only absent, but the opposite state of affairs existed. He was forced to follow this course, knowing the dangers, but as his partner was an officer in France, he felt it to be his duty to conduct the business even to his own detriment. Potassium iodide and mercury have been faithfully followed for fourteen months. He was given six intravenous injections of arsphenamin 0.2 gm. during the first six weeks and two courses of three injections of 0.3 gm. at weekly intervals in October and November, 1918. There was no reaction after any of these injections. The dyspnea had disappeared by the time he left the hospital, but he continued to have some thoracic pain for two months longer, but this was very mild in comparison to what it had been. He has reported about once a month up to the present time. At this date, which is fourteen months after the treatment

began, he is much improved. He occasionally has had slight thoracic pain, but it is a very infrequent occurrence now. There is no dyspnea. He is able to sleep readily, a thing which one year ago was impossible. To use his own words, "He feels 100 per cent. better today than one year ago." The physical signs, however,

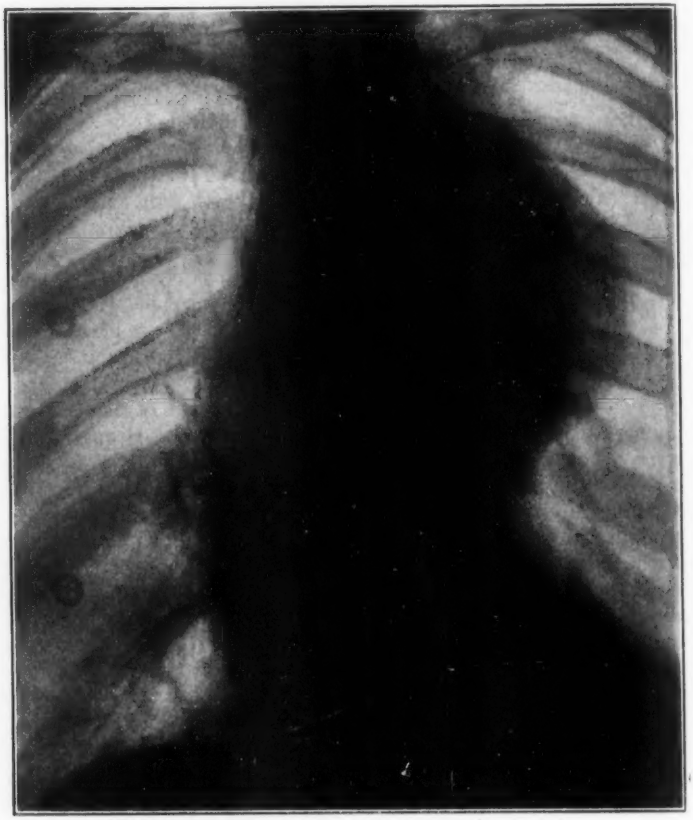

FIG. 4.—Case III. Plate taken fourteen months after the beginning of treatment. (The first roentgen ray at the time of admission was broken, but the report on it would indicate a shadow of somewhat the same type as the above.)

really do not show much change. The roentgen-ray shadow is of an alarming size. There is a very definite diminution in the visible thoracic pulsation, but otherwise the signs are about what we described. The Wassermann is negative. He has gained twenty pounds since the treatment began. We intend to give more arsphenamin, and of course continue the mercury and iodide for a

year or more at least. The aneurysm in this patient is also a large one. At the end of fourteen months he is certainly in much better shape, having put on twenty pounds in weight, and now being practically free from symptoms. The diminution in the heaving pulsation over the upper chest, which was most marked one year ago, is very noticeable. This is about the only outstanding change in the physical signs. He is fortunately now situated in such a way that he will be able to take more rest. Here, again, the general improvement after a period of over one year is rather more than one would expect from a case of this type.

Discussion. We frankly admit that our cases are too few in number and the time under treatment too short to allow us to make any dogmatic statement on the prognosis of this disease. The opportunity to study cases of this type for considerable periods is not always available, and therefore one must make the best of what is to be had. It is easy enough to observe a fair number of aneurysms, as the condition is by no means uncommon; but in our experience it has been a very difficult matter to keep in touch with these patients. In order to estimate the ultimate value of a *regime* such as we have suggested, it is necessary to follow a number of cases for several years.

We wish to emphasize, however, the general improvement noticed in three cases of aneurysm, two of them of massive size, after a period varying from fourteen months to three years. We are at present inclined to feel that the absence of symptoms, the ability to do the day's work and the general improvement in health are to be taken as the index of the results of therapy. The changing of the Wassermann reaction at the end of the first year is important, but of much more value is the negative Wassermann at the end of several years. We regard it as being very unwise to stop treatment too early on account of a negative complement-fixation.

The physical signs of a dilated aorta and the lack of any special change in the roentgen-ray picture might at first be considered as proving the failure of therapy. This, however, may not be the case. After an aneurysm has developed it is most likely an impossibility for the normal ever to return, and hence the shadow cast is going to be more or less as before. With early sacculations one might expect considerable alteration in the size after treatment, but we hardly look for any change in aneurysms of the size of our last two cases. The roentgen-ray plate does not indicate whether the inflammatory process in the wall has subsided or not. In fact, there is no way of being sure of this point at the present time. As long as the aortic enlargement does not appear to be increasing in size, and associated with this there is a general improvement in the patient we are not going to worry over the fact that the sac shows no signs of returning to the normal. In Case II there was a visible mass in the chest wall which disappeared, but this may not mean

that the whole sac was any smaller. The development of what does appear to be a fine layer of calcium in the sac of the first case three years after treatment began is of interest from several points of view. In the first place calcification and syphilitic lesions of the aorta do not, as a rule, go together. One sees very few aneurysms at autopsy showing any evidence of calcification in their walls. It would be very interesting to know whether the so-called spontaneously healed aneurysm, which we know occurs, has calcium deposits in its wall, and also whether a positive history of syphilis is present. One is tempted to ask if in our case this deposit bears any relation to or is an index of healing. At the present time, however, we are able to do little more than note its occurrence.

We must admit that we are favorably impressed with the results so far observed, and therefore feel justified in recommending more active antisyphilitic treatment for aortic aneurysm.

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7. Winternitz: Johns Hopkins Hosp. Bull., 1913, xxiv, 212.

THE SIGNIFICANCE OF YELLOW SPINAL FLUID.

By Charles H. Nammack, M.D.,

ASSISTING VISITING PHYSICIAN, BELLEVUE HOSPITAL, N. Y.; PATHOLOGIST, NEW YORK HEALTH DEPARTMENT AND NEW YORK DISPENSARY; INSTRUCTOR IN CLINICAL MEDICINE, CORNELL UNIVERSITY MEDICAL COLLEGE.

The occurrence of a yellow spinal fluid is sufficiently rare as to excite interest and sufficiently common to merit a brief consideration of its significance. The true syndrome of Froin[1] consists in (1) a spinal fluid which coagulates at once or upon standing—the consistency of the clot varying, but often so tenacious as to permit one to invert the tube; (2) a yellow coloration or xanthochromia; (3) a marked increase in cells and albumin. Froin[2] and all others who have studied this condition are agreed that the coloration is due to the presence of blood pigments chiefly bilirubin and the increased coagulability to an increase in fibrin. We shall not attempt to review the causative factors, mechanical and clinical, that bring

[1] Gaz. des hôp., Paris, 1903.
[2] Syndrome de Coagulation Massive, Gaz. des hôp., 1908, p. 1587.

about this departure from the usual pathological findings in spinal fluids but proceed to a consideration of the conditions in which it is encountered.

In a description of 100 cases Sprunt and Walker[3] state that the majority of cases showing yellow fluid present the complete syndrome but in 96 cases we have only had it occur in six instances. It appears that the true syndrome of Froin represents the highest development of a process in the spinal fluid of which the yellow coloration without the other essentials represents the earliest stage. Our 6 cases that presented the complete syndrome were 2 meningeal hemorrhages, 2 cases of tuberculous meningitis, and 2 of poliomyelitis.

In 95 cases of cord tumors and other chronic surgical conditions of the spinal cord which Elsberg and Rochefort[4] studied at the Neurological Institute, New York City, they found yellow fluid in 14 cases and spontaneous coagulation in 7 cases—a rather high proportion which would lead me to believe that disease of this kind tends to produce the conditions necessary for the development of the complete syndrome of Froin as stated by Mestrezat[5] to wit: (1) the existence of a closed cavity shut off from the general circulation in which the elements derived from blood accumulate (by transudation or hemorrhage); (2) an alteration (infectious or toxic) of the vessels of the cavity bringing about a transudation or a number of minute hemorrhages. In Dr. Elsberg's series of cases in which yellow fluid occurred, there were ten extramedullary tumors, two gummas, one varicose vein of the cord, and one neuritis of the cauda equina.

Our series of cases, 96 in all, represent the number of instances in which these cases have occurred in nine years of work of the Meningitis Division of the Health Department. There were 5801 fluids so that the percentage of cases in which yellow fluid occurred was about 1.6 per cent. Of these 96 cases, 60 have been tabulated and accompany this paper in the form of a table which is appended. Thirty-six cases were omitted from tabulation because the diagnosis was never confirmed definitely or there was lack of sufficient data. The chief interest of our series of cases lies in the fact that we see almost exclusively acute or subacute types of disease—which probably accounts for the small number of cases in which the syndrome of Froin occurred in all its manifestatins. Our cases were as follows: tuberculous meningitis 40, poliomyelitis 13, cerebral hemorrhage 3, meningeal hemorrhage 1, cord tumor 1, pachymeningitis 1, cerebrospinal meningitis 1.

Yellow fluids occurred in many cases of recovering epidemic meningitis but were omitted from consideration in this paper

[3] Significance of Xanthochromia of the Cerebrospinal Fluid, Bull. Johns Hopkins Hosp., 1907, xxviii, 80.

[4] Xanthocromia and Other Changes in the Cerebrospinal Fluid, Jour. Am. Med. Assn., vol. lxviii.

[5] Le Liquide Cephalorachidien, Paris, 1912.

TABLE OF YELLOW FLUIDS.

No.	Amount, c.c.	Coagulation.	Albumin.	Globulin.	Fehling's.	Cells, per cent.	Diagnosis.
1	60	0	++1 solid	++ solid	+1	+ 95 (polys.)	Tb. meningitis.
2	15	+++	+++++	+++++	+1	++95 (monos.)	Poliomyelitis.
3	15	0	++++	+++	+	+95 (monos.)	Poliomyelitis.
4	10	0	++++	+++	++	+95 (monos.)	Tb. meningitis.
5	5	0	+++	++++	0	+90 (monos.)	Tb. meningitis.
6	8	0	+++	++	N.d.	None (?)	Poliomyelitis.
7	3	0	++	+++	N.d.	+	Tb. meningitis.
8	20	0	+++	+++	N.d.	+90 (monos.)	Tb. meningitis.
9	40	0	+	+	N.d.	Red blood cells	Meningeal hemorr.
10	8	0	+++	+++	N.d.	+95 (monos.)	Tb. meningitis.
11	3	0	++++	++++	N.d.	+95 (monos.)	Tb. meningitis.
12	8	0	+++	++++	+	+60 (monos.)	Poliomyelitis.
13	40	0	+++	+++	0	+50 (monos.)	Tb. meningitis.
14	70	0	+++	++	N.d.	90 (monos.)	Tb. meningitis.
15	10	0	++	N.d.	N.d.	Few cells	Pachymeningitis.
16	5	0	++	+++	N.d.	++	Poliomyelitis.
17	5	0	++++	++++	+1	+90 (monos.)	Tb. meningitis.
18	10	+	++++	++++	+1	+98 (monos.)	Tb. meningitis.
19	40	0	+++1	++++	+	+95 (monos.)	Tb. meningitis.
20	30	0	++++	++++	+1	++90 (monos.)	Tb. meningitis.
21	20	0	++++	++++	+	+90 (monos.)	Tb. meningitis.
22	20	0	++++	++++	++1	+90 (monos.)	Tb. meningitis.
23	30	0	++++	++++	++1	+80 (monos.)	Tb. meningitis.
24	25	0	++++	++++	++1	+95 (monos.)	Poliomyelitis.
25	15	0	++++	++++	+1	+70 (polys.)	Tb. meningitis.
26	10	0	++++	++++	++	+90 (monos.)	Tb. meningitis.
27	25	0	+++++	+++++	+	+90 (monos.)	Tb. meningitis.
28	35	0	++++	++++	+1	+90 (monos.)	Tb. meningitis.
29	5	0	++++	++++	++1	+90 (monos.)	Tb. meningitis.
30	5	+	N.d.	++++	−	Few	Meningeal hemorr.
31	2	0	++++	++++	+1	+ Slight +	Tb. meningitis.
32	5	0	++++	+++	+++	90 (monos.)	Cerebral hemorrhage.
33	30	0	+	+	+++	++	E. C. S. W.
34	35	0	++++	++++	+1	+90 (monos.)	Tb. meningitis.
35	20	++	+++++	++++	++	+70 (monos.)	Meningeal hemor.
36	20	0	++++	++++	+	+mod. 90 (mon.)	Tb. meningitis.
37	20	0	++++	++++	+	+80 (monos.)	Tb. meningitis.
38	3	.	++++	++++	N.d.	N.d.	Poliomyelitis.
39	20	0	+++	+++1	+++	+60 (monos.)	Poliomyelitis.
40	10	0	++++	++++	+1	+95 (monos.)	Tb. meningitis.
41	20	0	++++	++++	0	+98 (monos.)	Tb. meningitis.
42	5	0	+++++	+++++	+	+89 (monos.)	Tb. meningitis.
43[6]	30	0	++++	++++	+++	Moderate +	Poliomyelitis.
44[7]	25	0	++++	++++	+++	+ monos.	Poliomyelitis.
45[8]	40	0	++++	++++	+	+90 (monos.)	Tb. meningitis.
46	30	0	++++	++++	+	+90 (monos.)	Tb. meningitis.
47	2	0	++++	N.d.	N.d.	+	Tb. meningitis.
48	3	0	++++	+++	+1	+90 (monos.)	Tb. meningitis.
49	10	0	+++	+++	+	+99 (monos.)	Tb. meningitis.
50	20	0	+++	+++1	+	+95 (monos.)	Tb. meningitis.
51	40	0	+++	+++	+++	+90 (monos.)	Poliomyelitis.
52	20	0	+++	++1	+	+mod. 95	Tb. meningitis.
53	15	0	+++	+++	+++	N.d.	Cerebral hemorrhage.
54	10	0	++++	+++	+++	+90 (monos.)	Tb. meningitis.
55	30	0	++1	++1	+1	+50 (monos.)	Poliomyelitis.
56	60	0	+++	+++	+1	+99 (monos.)	Tb. meningitis.
57	15	0	++++	++++	+	+95 (monos.)	Tb. meningitis.
58	15	0	++++	++++	++++	+75 (monos.)	Poliomyelitis.
59	30	0	+++	++	++	+90 (monos.)	Tb. meningitis.
60	30	0	++	+++	+	+99 (monos.)	Tb. meningitis.

[6] Fluid No. 43, gold chloride curve, 1111, 232100.
[7] Fluid No. 44, gold chloride curve, 111, 22332210.
[8] Fluid No. 45, gold chloride curve, 111, 2322100.
N.d., not done.

Summary:

Tuberculous meningitis	40
Poliomyelitis	13
Cerebral hemorrhage	3
Epidemic meningitis	1
Pachymeningitis	1
Syringomyelia	1
Meningeal hemorrhage	1
Total	60

because the condition did not occur spontaneously but after the administration of serum, which, however, we do not consider the cause of the xanthochromia.

Mestrezat[9] and many of the French writers have pointed out that the occurrence of a yellow fluid is not uncommon in tuberculous meningitis, yet it forms a very striking fact that it occurs in over $66\frac{2}{3}$ per cent. of our cases. Neal and DuBois[10] have already pointed out that yellow fluids occur too in poliomyelitis.

It had long been my clinical observation which is confirmed by these figures that given a patient with meningeal symptoms who on lumbar puncture shows yellow spinal fluid one should be inclined to a diagnosis of tuberculous meningitis or poliomyelitis—this evidence, of course, being by no means conclusive but merely a factor to be considered in the other points of diagnosis which further study of the spinal fluid usually decides.

The spinal fluid withdrawn in these cases has varied in amount from 3 c.c. to 50 c.c. The color has ranged from the faintest of yellow tints to the deepest canary. The albumin and globulin have been markedly increased in the majority of the cases. The sugar reactions as shown by the reduction of Fehling's solution has varied with the underlying etiological infection. In three instances colloidal gold curves were performed and these are included in the table.

RÉSUMÉ. (1) Yellow spinal fluid occurs in a wide range of diseases of the spinal cord and meninges; (2) the complete syndrome of Froin is comparatively rare in its occurrence; (3) in acute or subacute conditions the presence of yellow fluid strongly suggests the probable diagnosis of tuberculous meningitis or poliomyelitis.

THE OCCURRENCE OF GLYCOSURIA IN MUSHROOM-POISONING, WITH THE REPORT OF FIVE CASES IN WHICH A MILD NEPHRITIS AND A RENAL GLYCOSURIA WERE THE PERSISTENT AND PREDOMINATING FEATURES.

BY M. E. ALEXANDER, M.D.,

RESIDENT PHYSICIAN, WATERBURY HOSPITAL, WATERBURY, CONN.

ALTHOUGH the history of mushroom-poisoning reaches back to the times of Babylonia and ancient Rome, most of the reports, even the more recent, give but little clinical details and no accurate account of postmortem findings. In reviewing the literature one is also impressed by the few reports of cases that have ended in recovery. Although recent investigators, as Clark, Marshal and

[9] Same.

[10] The Diagnosis of Poliomyelitis, AM. JOUR. MED. SC., September, 1916.

Rowntree,[1] have emphasized the urinary findings and the blood chemistry in cases of mushroom-poisoning,[2] I can find no reference to the occurrence of glycosuria in such cases. In a personal communication from Dr. Carl Th. Mörner of Upsala, who recently published an exhaustive treatise on poisonous mushrooms (*Om de Högre Svamparna*, Upsala, 1919), he writes that he has never met with a case of glycosuria following mushroom-poisoning, nor has he read any account of it in his review of the literature.

It is not necessary in this place to review the history of mushroom-poisoning. The subject has recently been reviewed by Mörner in *Upsala Lakareforenings Forhandlingar*, January 20, 1919, pp. 1 to 57, also in the work mentioned above. It may be of interest to note that one of the earliest clinical reports in the literature is by Cheney,[3] although no postmortem findings are given. Caryon,[4] in 1873, reported the clinical course of a fatal case, and Adolph Kessler,[5] in 1880, reported the urinary and clinical findings of acute nephritis in a fatal case, as was also proved at autopsy. Michel[6] reported some cases in 1876, Ore,[7] in 1877 and Plowright,[8] Palmer,[9] and McGlenn[10] in 1879. Schröter[11] and Trask[12] also reported cases in 1883. Studer, Sahli and Schärer,[13] in 1884, collected all previous cases of poisoning that had autopsies performed and also reported several new cases. The pathological findings generally encountered were ecchymoses and hemorrhages in serous membranes and parenchymatous organs, together with profound fatty degeneration in liver and kidney. The heart may be found in a state of dilatation. The lungs are congested and bronchopneumonia of the hemorrhagic type is frequently encountered.

Although acute nephritis has long been recognized as a manifestation of mushroom-poisoning, it is only recently that a careful study of the urine and blood was undertaken by Clark, Marshall and Rowntree.[14] In none of their cases was there any evidence of any nitrogen retention in the blood. The phenolsulphonephthalein output was generally quite low, 33 per cent. in one of the cases that recovered.

In the cases forming the basis of the present paper, glycosuria was present in addition to the evidences of a mild nephritis.

[1] Jour. Am. Med. Assn., April 10, 1915, pp. 1230–1232.
[2] By Amanita Phalloides.
[3] Cases of Mushroom-poisoning, Pacific Med. and Surg. Jour., 1871–2, v, 119–121.
[4] Gaz. des hôp., 1873, p. 1146.
[5] Fatal Poisoning by Mushrooms, Am. Jour. Med. Sc., October, 1880, pp. 393–399.
[6] Gaz. hebd. de méd., 1876, p. 657.
[7] Compt. rend. Soc. de biol., lxxxiii, 837.
[8] Lancet, December, 1879, p. 941.
[9] Toadstool-poisoning, Boston Med. and Surg. Jour., ci, 301–304.
[10] Six Cases of Toadstool-poisoning, Med. Herald, Louisville, 1879–1880, i, 255.
[11] Breslauer Aertzl. Ztschr., 1883, p. 149.
[12] Cases of Mushroom-poisoning, Am. Jour. Med. Sc., 1883, lxxxv, 358–365.
[13] Beiträge zur Kentniss der Schwammvergift., Mitteil. der Naturf. Gesellsch., Bern, 1884, p. 85.
[14] Mushroom-poisoning, Jour. Am. Med. Assn., April 10, 1915, pp. 1230–1232.

The five cases occurred in one family. The father was aged forty-nine years; the mother, forty-eight; a daughter, twenty-one; a son, sixteen; and a boy, aged five. The mushrooms, about a pound by weight, were picked in the forenoon of August 28. They were boiled and prepared with milk and butter. It was said that the number of mushrooms consumed by each member of the family was in proportion to age, for the father ate most and the mother and children lesser amounts. About three hours after the ingestion of the mushrooms the father complained of nausea and of pain in the epigastrium. Soon afterward all the others had a similar experience. About two o'clock that morning they all vomited and complained of headache and dizziness. Their vision was blurred and the sensorium somewhat confused. The vomiting persisted all night, each one having vomited eight to ten times. Toward morning they felt a little better and that day they all pursued their daily occupations. For three days they all felt fairly well, although each gives a history of having felt weak, being nauseated and suffering from headache. Their appetite was poor and they ate but little, but took no particular care with their diet, having eaten anything they desired. Gradually their condition became worse and on the fourth day after the ingestion of the mushrooms their headache became intense and they complained of an unpleasant taste in the mouth and marked thirst. They all again commenced to vomit and were markedly prostrated. The father, who seemed most affected at this time, was advised to enter the hospital. He was admitted to the Waterbury Hospital, in the service of Dr. Engelke, on the fifth day after the ingestion of the mushrooms.

The physical examination revealed a well-nourished male, aged about forty years, five feet nine inches tall, and weighing 160 pounds. He was rather pale and the scleræ were slightly jaundiced. The heart and lungs were negative. There was no edema of the extremities and the reflexes were normal. The temperature at the time of admission was 98.4° F.; pulse 80, respirations 20. The blood-pressure was: systolic 128 and diastolic 80. The blood examination showed the hemoglobin to be 85 per cent.; red blood cells, 4,400,000; white blood cells, 8100; polynuclears, 74; lymphocytes, 22; mononuclears and transitionals, 3; eosinophiles, 1. The alveolar air was 35 per cent., determined by the Marriott method.

The urine was cloudy; yellow; 1024; acid; heavy cloud of albumin, 0.75 per cent.; sugar; marked reduction of the Benedict-Fehling reagent (quantitative determination, 2.5 per cent.). The microscopic examination showed amorphous urates and numerous finely and coarsely granular casts, also an occasional white blood cell. There was also a moderate trace of acetone and a faint trace of diacetic acid. There was no increase of indican.

The secretion of urine during the next twenty-four hours was 1700 c.c. The specific gravity was 1022; acid; slight cloud of

albumin, 0.25 per cent.; total, 4.25 gm.; sugar, 2.5 per cent.; total, 38.25 gm.; urea, 0.008 gm. to 1 c.c., total, 13.6 gm. The microscopic examination showed numerous granular and occasional hyaline casts also an occasional white blood cell. There was a marked reaction for acetone and a heavy trace of diacetic acid. The indican reaction was normal.

KIDNEY FUNCTION, ETC., OF C. S. (CASE STUDIED IN HOSPITAL).

Date.		Urine.						CO_2 alveolar air.	Blood.				Phenolsulph. test, per cent.
		Albumin.	Sugar.	Casts.		Acetone.	Diacetic.		Urea nitrogen.	Creatinin.	Uric acid.	Sugar.	
				Hyaline.	Granular.								
Sept.	1	0.5	2.5	occas.	num.	++	+	30	40	1.6	1.0	90	15
	3	0.5	2.5	"	"	+++	++	25					
	5	0.25	2.25	"	"	++	+	35					
	7	0.25	2.25	"	"	+	0	35	32	1.4	0.8	80	20
	9	0.12	2.0	"	"	0	0	40					
	11	0.1	1.25	few	mod.	0	0	45					
	13	v. f. t.	0.75	"	"	0	0	45					
	15	v. f. t.	0.25	"	few	0	0	45	25	0.8	1.0	70	30
	17	v. f. t.	0.24	"	"	0	0	45					
	19	v. f. t.	0.12	"	"	0	0	45					
	21	0	0.12	"	0	0	0	45	22	0.4	0.8	65	35
	28	0	0	"	0	0	0	45					60
Oct.	5	0	0	0	0	0	0	45	16	0.4	1.2	70	65
	19	0	0	0	0	0	0	45	14	0.5	..	80	80

The subsequent urinary findings, together with the blood chemistry and other laboratory examinations, are set forth in the accompanying table. As will be seen from this tabulation the glycosuria was more prominent and more persistent than the albuminuria. There was a very slight retention of urea nitrogen, and creatinin in the first two determinations. The sugar content of the blood was decidedly normal throughout. The phenolsulphonephthalein output was very low at first and remained low even after the urine showed no albumin and no casts.

On the fifth day after admission the patient was given 100 gm. of glucose and the urine was examined quantitatively every hour. The sugar output varied from 2.5 per cent. to 2.25 per cent. There seemed to have been no increase in the sugar output in the urine following the ingestion of the glucose; since the day before similar quantitative determinations made every hour showed a similar slight variation. Seven days later these tests were repeated, with the same results.

As regards the patient's symptomatology for the first forty-eight hours after admission to the hospital, he complained of considerable headache, nausea and marked weakness. He was given a saline cathartic and the rest of the treatment was that of a mild nephritis.

Potassium acetate and potassium citrate, āā gr. x, were given every four hours. His diet consisted of milk, cereals and cooked vegetables. Spices, broths and meat extracts were prohibited. The glycosuria was considered a secondary manifestation and no special attempt was made to deny the patient carbohydrates. As can be seen from the accompanying chart the urine has returned to normal at the end of the fourth week, although the subjective symptoms disappeared shortly after admission to the hospital.

The symptoms, urinary findings and entire course of the other four patients that partook of the mushrooms were exactly similar to those of the father, as already described. The urinary picture of one was almost exactly the same as of any of the others. There was the same amount of albumin and the same predominance of granular casts and scarcity of hyalin. The mother's urine had 2.5 per cent. sugar; the daughter, 2.75 per cent.; the son, 2.5 per cent.; the boy, 2.25 per cent. Even the duration was exactly the same, four weeks having elapsed before the urine entirely cleared up.

Among the mushrooms that were left uncooked there was one specimen that was identified by Professor Lafayette B. Mendel, of Yale, as an Amanita muscaria. The rest were Agaricus campestris. Two other people ate everything at that meal except the mushrooms, and they had no untoward symptoms whatsoever.

It is well known that in addition to phloridzin there are numerous chemical substances that may produce glycosuria. To enumerate them briefly one may mention the caffein group,[15] curare,[16] strychnin,[17] carbon monoxide poisoning,[18] amyl nitrite,[19] chloral,[20] sodium chloride,[21] phosphorus-poisoning[22] and several others. Recently, Salant and Wise[23] produced glycosuria experimentally by means of the zinc salts.

The phloridzin diabetes has been the one most thoroughly investigated. Since von Mehring[24] first reported upon it in 1886 numerous investigators have repeated and amplified upon his findings. It was not only demonstrated that phloridzin acts upon the kidney substance by lowering its permeability point to sugar, but it was also shown what part of the kidney is acted upon. In con-

[15] Jacobi, C.: Ueber künstlichen Nierendiabetes, Arch. f. exp. Path. u. Pharm., Leipzig, 1894–95, xxxv, 213–221.

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[22] Laub, M.: Wiener med. Wchnschr., January 13, 1898.

[23] Production of Glycos by Zinc Salts, Jour. Biol. Chem., May, 1918, xxxiv, 447.

[24] Ueber exp. Diabetes, Verh. des Cong. f. inn. Med. Wiesb., 1886, v, 185–189.

nection with his studies of experimental diabetes, von Mehring shows that in phloridzin diabetes the blood shows no hyperglycemia. Clinically, also, renal diabetes is characterized by no increase in the blood sugar. When, in 1896, Klemperer[25] reported a case which he called "renal diabetes," he stipulated that in order for such a diagnosis to be made the following postulates must be fulfilled:

1. The glycosuria must be independent of the amount of carbohydrates ingested.
2. There must be no increase of sugar in the blood.
3. The development of a nephritis decreases the glycosuria.

Subsequent investigations of these cases of "renal diabetes" showed that the second postulate is absolutely correct, but the first and third are not necessarily to be fulfilled. The characteristics of renal glycosuria have been succinctly stated by Allen[26] as "Glycosuria, with normal glycemia, relatively independent of diet."

The literature on this subject has recently been reviewed by Bailey,[27] and Lewis and Mosenthal[28] have given an excellent review of the cases so far reported.

It will, hence, be seen that the cases of glycosuria in mushroom-poisoning described above will very likely fall into the group of renal glycosuria.

PULMONARY COMPLICATIONS OF PARATYPHOID FEVER, WITH A REPORT OF FOUR CASES.

By Thomas Klein, M.D.,
INSTRUCTOR IN MEDICINE, UNIVERSITY OF PENNSYLVANIA,
AND
Robert G. Torrey, M.D.,
ASSOCIATE IN MEDICINE, UNIVERSITY OF PENNSYLVANIA.

During the past four years we have had the opportunity of studying 6 cases of paratyphoid fever, and of these 4 have been associated with severe pulmonary disturbances during the course of the paratyphoid infection. In the army during this same period much attention has been paid to the prevention of the disease in the way of sanitation and by protecting the individual by a prophylactic immunization in using the triple vaccines, but the detection of chronic carriers has not had the emphasis put upon it that it deserves. It is in the civilian population that these periodic outbreaks of the paracolon infections, probably due to chronic carriers, will occur from time to time.

[25] Verein. f. inn. Med., Berlin, May 18, 1896.
[26] Glycosuria and Diabetes, Boston, 1913, p. 544.
[27] Renal Diabetes, Am. Jour. Med. Sc., No. 2, clvii, 221–236.
[28] Johns Hopkins Hosp. Bull., 1916, xxvii, 133.

In the late winter months of 1915 our attention was called to the association of pulmonary lesions in paratyphoid fever in a young adult male admitted to the wards of Dr. Joseph Sailer, with frank lobar pneumonia. His condition progressed favorably and his lungs entirely cleared, but the fever still persisted. The pneumonia was of short duration, and we were much puzzled by the continuance of the fever with an otherwise complete symptomatic recovery. The man was not septic and the blood culture was negative at this time. In the course of a few days the patient had a large hemorrhage from the bowels, followed by several small hemorrhages. At this time the Widal reactions for Bacillus typhosus and Bacillus paratyphosus A were negative, but it gave a strong, positive agglutination for Bacillus paratyphosus B. The blood culture again was negative. The second series of agglutination tests confirmed the first, and subsequently the Bacillus paratyphosus B was isolated from the stools. The patient made an uneventful recovery. This case stimulated our interest in the subject, and since that time we have had the opportunity of observing 3 additional cases showing pneumonic complications occurring among the 5 cases observed by us since that time.

It was not until Achard and Bensaude,[1] in 1896, isolated the bacillus and reported 2 cases, which they called *fièvre paratyphoïdique*, that the disease was recognized as a distinct entity. Widal and Notecourt, in 1897, were successful in isolating the same bacillus from a post-typhoidal abscess. Gwyn,[2] in 1898, was the first to isolate and culture the Bacillus paratyphosus from the blood during life. From this time until 1902 we find but 24 cases reported in the literature; these do not include the Saarbrücken epidemic of 38 cases, as they were not bacteriologically certain to be paratyphoid fever. It is of interest to note that at this time the reports included cases from Germany, France, England, the United States and the Philippines, showing the wide geographic distribution of the infection. This same year Longscope[3] reported 2 cases, with autopsy records of 1, in which he stated the presence of extreme congestion and moderate edema of the lungs. Herpes labialis was present in both his cases. Coleman[4] also reported that herpes occurred in 50 per cent. of the cases and stated that a mild bronchitis was one of the initial symptoms. Bronchopneumonia was also mentioned as a complication at that time. He quotes an epidemic in Middlesboro, in 1888, caused by eating poorly cooked pork in which pleuropneumonia was quite frequent. Autopsy confirmed the clinical manifestations. Coleman was of the opinion that this epidemic was caused by one of the paracolon group, probably the Bacillus psittacosis.

[1] Bull. et mém. Soc. méd. de hôp., Paris, 1896, xiii, 820.
[2] Johns Hopkins Hosp. Bull., 1898.
[3] Am. Jour. Med. Sc., 1902.
[4] Am. Med., 1902, iv, 498, 578, 622.

In 1909 Proescher and Roddy[5] report an epidemic of 48 cases in Pittsburgh in which cough and bronchitis occurred in 12, or 25 per cent. Acute catarrhal laryngitis was an early symptom. Pneumonia occurred in only one instance, and this patient had been home, sick in bed, for three weeks prior to admission. The pneumonia was lobar in type and involved both lungs. Hoskins,[6] in the epidemic at Wayne's Cave, Virginia, in the spring of 1909, reports a bronchitis of a persistent character, lasting for several days after the temperature had become normal, in 23 of the 35 cases. This epidemic was due to Bacillus paratyphosus B, while the Pittsburgh epidemic was due to Bacillus paratyphosus A. In our series of 4 cases 3 were due to the type B infection. In this country the outbreaks have been followed chiefly from a bacteriological standpoint and very few of the observers have mentioned the clinical manifestations.

In the spring and summer of 1916 we had the privilege of studying 2 cases of paratyphoid fever, both of the B. type and both associated with frank evidences of a bronchopneumonia—one of a lobar distribution while the other involved both lungs.

Case No. G, 3914. G. N., adult, male, aged twenty-five years, Italian, laborer, was admitted February 14, 1916, complaining that he had "caught cold," with pain in the lower part of the abdomen, headache and general weakness. Upon examination the patient looked very ill, had a temperature of 103° F., pulse 84 and respirations 30. The spleen was palpable and rose spots were present. Over the right lower lobe the percussion note was dull, the breath sounds exaggerated and many rales were present. Vocal resonance was also increased. Five days after admission his temperature became normal, to be followed the next day by spitting up a mouthful of blood, sharp elevation of temperature to 102.3° F., and an increase in the respiratory rate. The physical findings at the right base had become intensified and were those of a frank bronchopneumonia of the lobar type. At this time the blood culture was positive for Bacillus paratyphosus B. It was again positive for the same organism three days later. The patient recovered and, in all, the fever lasted nine days. The sputum was not cultured for the Bacillus paratyphosus.

This is the type of case which could easily be taken for any of the acute respiratory infections, and might easily become the source of an epidemic of paratyphoid fever.

Case No. 3. G. M., admitted August 22, 1916, complained of dizziness, anorexia, being unable to work and headache which had become worse three days prior to admission. On examination his teeth were in bad condition, tongue dry and coated. A respiratory grunt was noted, but the lungs were found to be clear except for a

[5] Jour. Am. Med. Assn., February 6, 1909, p. 470.
[6] Ibid., 1910, liv, 930.

few scattered rales below the angle of the scapula of the left side. The heart was normal. Splenic area of dulness was increased, but the spleen was not palpable. Rose spots were absent at this time. Temperature on admission was 103° F., pulse 82, respirations 40. Widal reaction for Bacillus typhosus was negative. The general condition remained the same for six days, when marked evidences of a very severe bilateral bronchopneumonia made their appearance. At this time the blood culture was positive for Bacillus paratyphosus B. His temperature continued for sixty-two days, but he finally made a complete recovery. During his illness his ears, which upon admission had shown a bilateral chronic purulent otitis media, were irrigated frequently each day, to keep them free from pus as nearly as possible. At this time, sixty-two days after admission and sixty-five days after the beginning of his illness, we were able to isolate the Bacillus paratyphosus B from the pus of the otitis media and also from around the teeth.

The finding of the bacillus in the discharge from an otitis media and from around the teeth indicates another means by which a patient may become a chronic carrier and through which the spread of the disease may take place.

During the war, epidemics of paratyphoid fever were rather frequent and were of sufficient magnitude to cause armies to be immunized against the infection by vaccination, however, much valuable data from a pulmonary standpoint had been collected in the interim. In October, 1915, Robinson[7] reported an epidemic of 89 cases in which the Bacillus paratyphosus had been isolated from the blood, feces or urine in 47 cases. The remaining 42 cases were clinically paratyphoid fever. Out of the 47 cases in which the bacteriological examination left no doubt as to the correctness of the diagnosis 23 gave a history of an initial chill; cough was present or had been in 26 of the 47 cases. The cough was nearly always loose in character and usually subsided rapidly. There was a history of doubtful hemoptysis in 2 cases. Definite signs of a bronchitis were recorded in 4 cases. Herpes labialis was recorded in only two case histories. Wiltshire[8] reports an epidemic of 98 cases in the British Expeditionary Forces. A positive bacteriological examination was obtained in 50 cases; 9 were due to Bacillus paratyphosus A and 41 were due to Bacillus paratyphosus B. In this epidemic pulmonary complications were present in 67.3 per cent. of the cases. Of these 33 had a slight generalized bronchitis, which occurred about the fourth day of the disease, while 19 cases had a frank bronchopneumonia and 5 were lobar in type. Of these 5 lobar pneumonias, 4 had acute pleurisies overlying the areas of consolidation. The fifth lobar patient developed an empyema and

[7] Lancet, October 16, 1915.

[8] Clinical Observations of Ninety-eight Cases of Paratyphoid Fever, Practitioner 1915.

died. No autopsy was performed and the culture from the empyema remained sterile, although the pus had the odor of a Bacillus coli infection. The sputum in these cases showed the pneumococcus, Micrococcus catarrhalis, streptococcus and influenza bacillus. As far as could be determined, the sputum was not cultured for the bacillus paratyphosus. In this series the men were only protected against the Bacillus typhosus by inoculation. Wiltshire was of the opinion that many of these cases could easily be mistaken for influenza or gastro-enteritis, as the attacks may be of short duration, in this way giving many opportunities for the carriers, as well as those actually sick with the disease, to spread the infection. Stolkind[9] describes a distinct respiratory form of paratyphoid fever in which the symptoms resemble those of influenza. He reports a case in Moscow, in 1916, in which the patient was suddenly attacked with a coryza, cough, headache, moderate fever and lassitude. The spleen was enlarged and rose spots were present. Bacteriologically the Bacillus paratyphosus was found. The fever lasted fourteen days. Beticeaw reports a similar case also occurring in Moscow. Baer observed an epidemic of paratyphoid B in 52 soldiers, all of whom had conjunctivitis and pharyngitis; many also had bronchitis. Grattan and Wood, and also Sufford, report cases of paratyphoid A occurring in British soldiers in India in which the attack might easily be mistaken for influenza. In half the cases there were sore-throat and bronchitis. Wilucki also reports an epidemic of 33 cases of paratyphoid bacillus in 7 of which the illness began with acute respiratory manifestations. Wilcox[10] describes a respiratory form of the disease and mentions that pneumonia of the bronchopneumonic type is not uncommon in the severe cases.

In France the army surgeons called attention to the same clinical phenomenon at this time. E. Joltrain et Petit Jean,[11] from the First Army, reported 19 cases of pleurisy occurring in 310 cases of paratyphoid fever. Of these 2 were due to empyema; 2 were dry pleurisies and the remaining 15 were serofibrinous. Of the 19 cases 18 were due to Bacillus paratyphosus B and 1 to Bacillus paratyphosus A. Also in our cases the Bacillus paratyphosus B type of infection seemed to be the one which gave us the greater number of pulmonary complications. In all cases the effusions were small, and cytologically they resembled a tuberculous pleurisy. The pleurisy was often the initial symptom, the paratyphoid infection being latent. This was also true in one of our cases of lobar pneumonia in which the paratyphoid had not been suspected until after the subsidence of the pneumonia. In this same connection Florenzano[12] believes that paratyphoid fever is always a septicemia, but

[9] Respiratory Form of Paratyphoid Fever, Lancet, January 15, 1916, p. 136.
[10] Lancet, February 26, 1916.
[11] Pleurisy in Paratyphoid Fever, Arch. de méd. et pharmacie Militaires, 1916.
[12] Gazzetta degli ospedali e delle cliniche, Milan, December 7, 1916, No. 98, xxxvii, 1537.

the main focus of infection may be in various organs in different cases. In a case described in detail the localization was in the pleura, and the symptoms of this had preceded the paratyphoid septicemia. The disease ran a course through a period of three months, the toxic and infectious symptoms recurring in three different attacks. In this series of cases pleurisy occurred in 6 per cent., while in typhoid fever the complication is noted in from 2 to 4 per cent.

From the pathological viewpoint, Saquépée, Burnet and Weiszenbach,[13] from the Fourth Army, report the macroscopic findings of 9 autopsies of cases in which the Bacillus paratyphoid A had been found before death. In all cases the pulmonary lesions in the form of intense congestion and edema were constant. There were also 2 cases of bronchopneumonia, 1 of a lobar type (left lower) and the other of a lobular type associated with a large empyema. Merklen and Trotain[14] report the autopsy findings in 15 deaths which occurred in 446 cases. Of these 10 were due to Bacillus paratyphosus B and 5 to Bacillus paratyphosus A. Pulmonary complications were the immediate cause of death in 6 cases. Again at this time Dawson and Whittingdon,[15] with the British Army, had 17 fatal cases of the disease, of which 2 were due to pneumonia. In 4 of the 17 cases the pulmonary complications were so severe as to predominate the clinical picture. Here again the Bacillus paratyphosus B death-rate was four times as great as that of the type A. A most important contribution to this phase of the disease has been made by Minet.[16] While working back of the French lines he was able to isolate and cultivate the Bacillus paratyphosus from the sputum in 7 cases, of these 4 were Bacillus paratyphosus A, 2 were Bacillus paratyphosus B and 1 was due to Gärtner's bacillus. In these cases the sputa were collected from intermittent bronchitis patients. In all cases the condition dragged along for several months, associated with emaciation, resembling chronic pulmonary tuberculosis. In one patient the condition localized itself to one apex of the lung, making its resemblance to tuberculosis still greater. Of great interest is the fact that one patient infected with Bacillus paratyphosus B who had completely recovered, contracted a Bacillus paratyphosus A infection by lounging upon the bed of an A type bronchitis patient. All cases under observation recovered.

Recently we have had admitted to our service at the Philadelphia Hospital a man, aged nineteen years, with a history of headache, diarrhea, general weakness and loss of weight. Examination showed the presence of herpes labialis, rose spots and an enlarged

[13] Macroscopic Study of Lesions Produced in Paratyphoid Fever, Arch. de méd. et pharmacie Militaires, 1916.
[14] Arch. de méd. et pharmacie Militaires, 1916.
[15] Quart. Jour. Med., London, 1916.
[16] Bull. de l'Acad. de méd., Paris, 1916.

spleen; temperature 103° F., pulse 100, respirations 28. A Widal reaction for Bacillus typhosus was negative. Four days after admission the patient's respiratory rate increased and he began to cough. At this time the sputum was very tenacious and blood-streaked. Remembering our experiences in the past with this type of case we immediately suspected a paratyphoid infection. The Widal reaction that day for Bacillus paratyphosus A was strongly positive. A blood culture was also positive for the same organism. The sputum was also cultured with a positive result. The Bacillus paratyphosus isolated from the sputum was agglutinated by the patient's serum. The pulmonary findings at this time were confined to the right lower lobe, and were bronchopneumonic. In addition to the paratyphoid bacillus in the sputum the pneumococcus was also present. The pneumonia, here again as in all our cases, was of short duration, lasting only four days. The patient at this time also had a series of small abscesses. The pus from these was cultured, but we were unable to isolate the bacillus. A few days after the subsidence of the pneumonia the patient developed a thrombophlebitis of the right leg, extending up to and including the external iliac vein. After the fever had subsided the pulse remained extremely rapid, ranging from 130 to 150 per minute. Soon after his thyroid became enlarged and at present there is an exophthalmos and a positive von Graefe. The Goetsch adrenalin test was applied with a positive result.

This case is of interest in showing that this disease can be as severe as a true typhoid fever, and that all complications of the latter disease can be found in association with paratyphoid fever. It also indicates that the sputum and nasal secretions of these cases should be collected and disinfected the same as the stools and urine. In a ward the possibility of cross-infections by means of cough must be borne in mind. In all cases in which the pulmonary symptoms are masked by an underlying condition the bacteriological examinations should always include those for the Bacillus paratyphosus.

In going over the records for the past five years at the Philadelphia General Hospital we found 15 cases of paratyphoid fever which had been diagnosticated bacteriologically. Of these 4 were type A and 11 were type B infections. The pulmonary complications were as follows: Lobar pneumonia, 1; bronchopneumonia (lobar in distribution), 3; bronchopneumonia (lobar in type), 1; acute bronchitis (severe), 1; acute bronchitis (mild), 2; dry pleurisy, 1; complicated by pulmonary tuberculosis with tubercle bacilli in the sputum, 1; no pulmonary complications, 5. Seasonal variations cannot account for the pulmonary complications, as 3 of the bronchopneumonias were admitted during the midsummer months. The shortest duration of the fever was nine days and the longest sixty-five days (a case complicated with

bronchopneumonia and a severe purulent otitis media). The age of the patients varied from fourteen to thirty-nine years. There was one death in the series, but no autopsy was made. This was due to a B. type of infection.

In conclusion, there seems to be a definite pulmonary form of paratyphoid fever which may be easily mistaken for any of the acute respiratory infections. The pulmonary symptoms and findings often precede any intestinal manifestations. Of the pulmonary complications, bronchopneumonia is the most alarming. As it has been shown that the bacilli are found in the sputum, we must recognize that bronchial infection may result in the patient becoming a chronic carrier as well as being a means of spreading the infection in the wards of a hospital. It is of interest to note that the bacilli have also been isolated from the purulent discharges of a chronic purulent otitis media, caused by other infections previous to the paratyphoid disease and that they were found as late as sixty-five days after the beginning of the illness. The organisms were also isolated from the secretions of a pyorrhea alveolaris. In view of Minet's findings and his ascribing the paratyphoid bacillus as the etiological factor in his cases of chronic bronchitis, it is worth while to examine the sputum of certain types of our chronic pulmonary invalids for this group of bacilli.

We wish to express our thanks to Dr. Joseph Sailer for the privilege of reporting two of the cases, as they occurred upon his service in the Philadelphia General Hospital.

A CASE OF PURPURA DURING SERUM DISEASE.[1]

By Henry Edmund Meleney, M.D.,
NEW YORK.

(From the Medical Clinic, Presbyterian Hospital, Columbia University, New York City.)

The following case of purpura which occurred during the course of serum disease following the use of antipneumococcus I horse serum in pneumonia is of such rare occurrence as to warrant its being reported.

S. M., Austrian, aged twenty years, clerk, was admitted to the Presbyterian Hospital on February 16, 1917, complaining of pain in the left chest, with chills and fever. The onset had been sudden the night before, with headache, cough, bloody sputum and vomiting. His family history was negative for chronic illnesses. He had had

[1] From the wards of the Presbyterian Hospital, New York City.

measles as a child but no other infectious diseases. He had never been given antitoxin of any kind. Three years before he had come to the Presbyterian Hospital dispensary because of the loss of twenty-five pounds in weight, with cough and night-sweats. No physical signs of tuberculosis were found in the lungs and no tubercle bacilli were found in the sputum. He had rapidly regained his lost weight and had been well until the present illness, except for an attack of "indigestion" six months before. There was no history of bruises, epistaxis, hematuria, bloody sputum, blood in the stools or skin eruptions.

On physical examination he was found to have consolidation of practically the whole left lower lobe. Cheeks were flushed, breathing was rapid and grunting, with frequent cough and glairy, bright red sputum. His heart was normal except for a rough systolic murmur localized to the pulmonic area. His abdomen was not distended. There was no skin eruption. Temperature 104.6° F., pulse 112 and respirations 34. Examination of the blood showed 21,600 white blood cells, with 90 per cent. polymorphonuclear leukocytes. Blood culture gave no growth of bacteria. The sputum was injected into a mouse, from which was recovered pneumococcus Type I.

Purpura occurring during serum disease. Note intensity of eruption below point of constriction of right arm by tourniquet.

Intracutaneous tests were performed with horse serum, using human serum and carbolized saline as controls. All were negative. One hundred cubic centimeters of antipneumococcus serum obtained from the Rockefeller Institute was given intravenously, diluted with 100 c.c. of normal saline. The patient experienced a slight chill, with dyspnea, which was relieved by atropin and adrenalin

given subcutaneously. His temperature rose from 104° to 105° and then fell gradually to 102° in the next eight hours. At that time another 100 c.c. of serum were given, with no discomfort to the patient. His temperature continued to fall, reaching 100° twelve hours later, when a third dose of serum was given. The following day his temperature was 98.6°, white blood cells 6100 with 77 per cent. polymorphonuclear leukocytes. The physical signs suggested the presence of free fluid in the left chest, which roentgen ray failed to confirm. Four days later exploration of the left chest recovered 10 c.c. of bloody fluid, which showed no organisms on smear and no growth on aërobic and anaërobic culture.

Seventh Day after First Serum Administration. A general slight enlargement of the lymph nodes appeared, with patches of erythema and urticaria scattered over the skin and numerous minute bright red petechial hemorrhages over the chest.

Tenth Day. The urticaria persisted, the lymph nodes were much enlarged and the inguinal nodes were quite tender. Face and eyelids were puffy. Patient complained of pain in both temporomandibular joints, in both shoulders and in the joints of both hands.

Eleventh Day. Patient complained of pain in all joints of his extremities except his ankles and feet. There was general slight swelling of all extremities. There was a diffuse papular erythema of the whole body. There was marked conjunctivitis in both eyes. A few urticarial wheals and new petechial spots were present. Temperature rose to 102.4°. The patient's blood showed the presence of precipitins for horse serum.

Twelfth Day. Throat was sore and diffusely red. Patient coughed up a little blood-tinged mucus. White blood cells were 13,600, with 87 per cent. polymorphonuclear leukocytes.

Thirteenth Day. Temperature, 104°. Cervical and inguinal nodes tender. At night the patient had a severe epistaxis, which was checked only by packing both anterior and posterior nares.

Fourteenth Day. Erythema somewhat faded, but many minute petechial spots appeared over thighs and chest. After the application of a tourniquet to the right arm above the elbow for venous puncture, a profuse purpuric eruption appeared all over the arm below the point of constriction. Skin and mucous membranes were now quite pale. Joint pains practically gone. Blood platelets, 315,000 per c.mm. Normal control, 330,000. Bleeding time, two minutes. Coagulation time, six minutes. Normal control, seven minutes. White blood cells, 10,600, with 83 per cent. polymorphonuclear leukocytes. Urine showed a faint trace of albumin and a negative guaiac test for blood.

Fifteenth Day. Petechial hemorrhages were present all over the body and in the mucous membranes of the mouth. There were several large submucous hemorrhages in the soft palate, probably

caused by trauma in packing the posterior nares. The lymph nodes were still quite tender. Erythema still present as well as a few new urticarial wheals. The spleen was palpable for the first time. Ophthalmoscopic examination revealed no hemorrhages in the choroid.

Sixteenth Day. Fresh petechial spots present on the shoulders and along scratch marks on the back. Red blood cells, 3,700,000; hemoglobin, 80 per cent. White blood cells, 6600: polymorphonuclear leukocytes, 79 per cent.

Seventeenth Day. Petechial eruption more extensive. Gums bleeding slightly. Spleen no longer palpable. Dark blood passed with a stool. Temperature, 101.6° to 103.4°.

Twenty-first Day. Temperature normal. General condition much better. Purpuric eruption gone except on buttocks and thighs. No more joint pains. Lymph nodes, especially one in the submaxillary region, still large but not tender.

Twenty-fifth Day. Temperature suddenly rose to 103.8°. Patient complained of difficulty in breathing and of very sore-throat. Swallowing very difficult, permitting the taking of fluids only. A hemorrhagic area was present on the left tonsil.

Twenty-sixth Day. Slight epistaxis. Petechial hemorrhages have all disappeared from the skin. Tourniquet applied to right arm for ten minutes produced no purpuric eruption. Lungs clear except for a few dry, inspiratory rales at the left base. Red blood cells, 4,300,000; hemoglobin, 60 per cent.; white blood cells, 19,000; polymorphonuclear leukocytes, 84 per cent.

Twenty-seventh Day. Nose and throat examined by Dr. Coakley. There was an area of ecchymosis on the right side of the nasal septum and on the right lower turbinate, possibly from the packing. The uvula was edematous, with diffuse capillary hemorrhages on the posterior surface. These extended to the posterior pillars of the fauces, which were very edematous. The anterior pillars were less so. Fresh blood was leaking from the left lateral pharyngeal wall, the point of origin not being visible. The epiglottis was very edematous on the left side, involving the left arytenoid cartilage. There was an ecchymotic area on the upper surface of the epiglottis. The vocal cords were congested.

Twenty-ninth Day. Slight epistaxis occurred. Another new petechial spot. Throat less edematous. Temperature rose in the afternoon to 104.6°. For the past few days every stool had contained either streaks or clots of blood.

Thirtieth Day. Temperature normal. Patient transferred to the hospital roof and felt much better.

From this time on the temperature continued normal and convalescence was rapid. No more petechial hemorrhages appeared and no more blood appeared in the stools. The swelling of the throat rapidly disappeared and the lymph nodes returned to their normal size.

Thirty-sixth Day. Precipitins for horse serum still present in patient's blood.

Thirty-seventh Day. Red blood cells, 4,100,000; hemoglobin, 60 per cent.; white blood cells, 9100, polymorphonuclear leukocytes, 61 per cent.

Fortieth Day. Patient discharged.

DISCUSSION. Schultz,[2] in discussing "Anaphylactoid Purpura," mentions three cases reported by Widmer[3] in which "purpura simplex" followed the administration of diphtheria antitoxin to small children. The only other case of purpura following the administration of serum, which we have been able to find in the literature is one reported by Flandin,[4] in which the subcutaneous administration of one dose of diphtheria antitoxin was followed thirteen days later, when the patient got up, by edema of the legs, arthritis with effusion, urticaria, erythema and purpura. The symptoms disappeared after rest in bed but recurred each time the patient got up. Calcium chloride and peptone injections had no effect on the recurrences, but finally minimal doses of normal horse serum (0.1 to 0.2 c.c.) given hypodermically, rapidly dispelled the symptoms. After this they reappeared mildly every two or three months and were each time relieved by small doses of horse serum. Each time the symptoms recurred the patient's blood serum was found to be toxic for a guinea-pig. After the injection of horse serum, however, this toxicity disappeared.

The occurrence of purpura during the course of these cases of serum disease seems to link serum disease etiologically more closely with the group of conditions commonly known as idiopathic purpura. The type of purpura observed in our case is not that which is characteristic of purpura hemorrhagica where there is a marked decrease in the number of blood platelets and where the bleeding time is greatly prolonged. (Platelets and bleeding time were both normal in our case.) But all these cases showed many of the features of the purpura which appear as a secondary manifestation of some of the acute infectious diseases or which occurs without any demonstrable cause or any abnormality of the blood elements. Osler[5] has followed many of these cases through varied manifestations of the disease, extending over many years and with several distinct attacks, some of which were associated with joint pains, some with abdominal pains, erythema, urticaria or even angioneurotic edema. Sometimes the purpura itself did not appear but the same pathological condition was suggested by the appearance of the other symptoms.

In the case reported we have the symptoms of both purpura

[2] Ergeb. d. Inn. Med. u. Kinderheilk., 1919, xvi, 32.
[3] Med. Klin., 1917, Nr. 39.
[4] Bull. et mém. Soc. méd. des hôp., 1914, xxx, 242.
[5] British Med. Jour., 1914, i, 517.

and serum disease and we have a known foreign substance in the blood and tissues (horse serum), which, either by its own presence or by the attempt of the patient to eliminate it, may be safely inferred to be etiologically associated with all of the symptoms. In our case there is considerable evidence that the purpuric eruption was due not to any abnormality of the blood but to some temporary lesion of the finer bloodvessels. The most marked eruptions occurred in regions which were most exposed to trauma, namely, the nasal and pharyngeal mucosa, the extensor surfaces of the arms, especially about the elbows, the buttocks, along scratch marks on the back, and especially on the arm below the site of constriction by a tourniquet which shut off the venous return and thereby caused distention of the capillaries. On the other hand, in places like the conjunctiva and retina, where trauma is not likely to be a factor, no hemorrhages occurred.

Bloodvessel lesions have been found in some experimental conditions in which capillary hemorrhages occurred. Gay and Southard[6] in their early studies in anaphylaxis found hemorrhages in the gastric mucosa, lungs, spleen, heart muscle, brain and several other organs of sensitized guinea-pigs, which had died of anaphylaxis following a toxic dose of horse serum. Associated with the hemorrhages they found focal fatty infiltration of endothelial cells of the capillaries. Flexner and Noguchi,[7] and later Pearce,[8] in studying snake-venom poisoning, also found lesions of the capillary endothelium associated with hemorrhages into various organs. The lesions here, however, were not fat infiltrations, but a swelling and lysis of the endothelial cells occurring focally and allowing extravasation of blood into the surrounding tissue. A third type of lesion of the capillary endothelium, which has been suggested as a possibility, from the result of a toxin introduced into the blood, is the dissolution of the so-called intercellular cement substance of the capillary endothelium, with extravasation of blood between the separated cells.

As no tissue from these cases was secured for microscopic examination the type of lesion in the capillaries, if one existed, can only be conjectured. In our case it is probable that any lesion which did occur was only temporary and lasted only as long as the effects of the toxic substance in the body continued. This is suggested by the fact that after the subsidence of the symptoms the application of a tourniquet to the arm no longer produced a purpuric eruption, as it had done during the height of the disease. The capillaries were again able to stand distention without rupturing. In Flandin's case, however, the lesion seems to have been much more permanent, for the symptoms recurred at intervals for an indefinite period and

[6] Jour. Med. Res., 1907, xvi, 143.
[7] Univ. Penna. Med. Bull., 1902, xv, 345.
[8] Pearce, R. M.: Jour. Exper. Med., 1909, xi, 532.

were only temporarily relieved by treatment. The toxicity of the patient's serum for a guinea-pig in his case seems to point to the production of a circulating toxin which periodically caused the appearance of the symptoms. Whatever the mechanism the evidence at hand suggests that the cause of some cases of purpura whose etiology is now so obscure may some day be demonstrated to be an intoxication following the introduction of a foreign protein into the body and therefore similar to the intoxication causing serum disease.

SUMMARY. 1. A case is described in which purpura occurred during the course of serum disease following the administration of antipneumococcus horse serum.

2. The elements of blood coagulation were normal, and it is therefore probable that the purpura was due to the presence of a toxin associated with the attempt of the body to eliminate the foreign protein.

3. The evidence points to the capillary walls as the site of the lesion.

4. Some cases of purpura of unknown etiology may be caused by the same type of intoxication which was present in this case.

PROGNOSTIC FACTORS IN PNEUMONIA DURING THE INFLUENZA EPIDEMIC.

BY JAMES H. SMITH, M.D.,
RICHMOND, VA.

THE title of this paper is purposely evasive. It speaks of "the influenza epidemic" because it is by that term that the disease which swept the world nearly a year and a half ago is generally known. In adopting the term it is with the mental reservation shared by many others as to the primary etiological factor. What part the Bacillus pfeiffer played is difficult to judge from the widely varying reports of equally skilled observers. It is not within the scope of this paper to discuss that question.

Again, many patients suffered at that time from the disease known as influenza without having a complicating pneumonia. On the other hand we know that the outstanding cause of death during the epidemic was an inflammatory affection of the lungs generally referred to as "pneumonia." When patients were seen at varying periods of their illness it was often—indeed usually—impossible to be sure that existing pneumonia had been ushered in by influenza. This uncertainty is expressed by the phrase "pneumonia occurring during the influenza epidemic."

It seems desirable to include a consideration of lobar pneumonia as well as the bronchial type, since a fair percentage of cases of the

lobar variety occurred during the epidemic, and necessarily, therefore, enter into the question of prognosis.

On this basis it is believed the situation can be reviewed in the light of the conditions that actually prevailed.

During the fall of 1918, Base Hospital 45, located at Toul, France, received 3965 cases diagnosticated as influenza or pneumonia. These affections seemed to agree in their main features with the pandemic disease prevailing at that time. As regards bacteriology the observations at this hospital align themselves with those reporting negatively as to any apparent role of the Bacillus pfeiffer as the causative agent of pneumonia. They agree with the frequently expressed opinion that, the question of primary etiology aside, the complicating pneumonia is attributable largely to streptococci and to a lesser extent to pneumococci, and that the mortality is attributable largely to the streptococcus, especially Streptococcus hemolyticus.

While circumstances necessarily affected the character of clinical studies made in the cases, the data are fairly complete in the series of 67 cases used as the basis for this report, and they may be accepted as representative of the larger number not included for lack of recorded data. No cases of pneumonia complicating gas inhalation are included. Our present purpose is to examine these 67 cases as to clinical, radiographical and postmortem features, with a special view to determining prognostic factors.

For purposes of discussion certain terms are used in connection with bronchopneumonia which will be defined. Clinically, on the basis of physical signs and roentgen-ray pictures, three varieties of bronchopneumonia will be referred to:

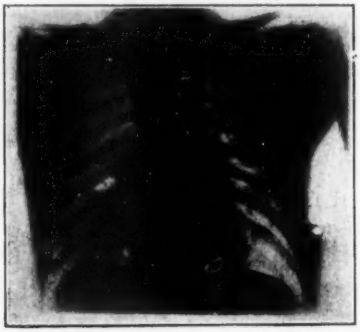

FIG. 1.—Illustrating the type of bronchopneumonia defined as "discreet."

DISCREET. To denote by physical signs limited, well-defined patches of pneumonia, few in number and of no great extension; and the same by the roentgen ray (Fig. 1).

DIFFUSE. Giving widely distributed signs, chiefly rales, bilateral, with no large areas of consolidation, showing by the roentgen-ray numerous, widely distributed, small areas of consolidation or diffuse, very small areas of consolidation closely resembling miliary tuberculosis (Fig. 2).

FIG. 2.—Illustrating the type of bronchopneumonia defined as "diffuse."

CONFLUENT. Showing by physical signs and roentgen-ray shadows widely distributed lesions, usually bilateral, not sharply defined, including on one side or both massive areas of consolidation (Fig. 3).

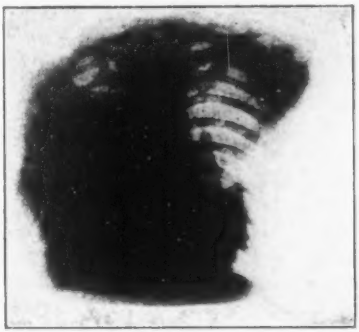

FIG. 3.—Illustrating the type of bronchopneumonia defined as "confluent."

The definitions are somewhat arbitrary. There was no sharp dividing line between the types. That kind of case designated "discreet" was clearly separable from the "confluent." But in an endeavor to separate an intermediate group, the "diffuse," borderline cases are encountered. In the two cases diagnosticated "diffuse" which died, confluent lesions were demonstrated at autopsy.

In contradistinction to all of these stands lobar pneumonia (Fig. 4), with its clear-cut, anatomical limitations, both to physical examination and the roentgen ray. And yet, even here, it is certainly possible to have a mixed type of infection, with a genuine lobar involvement and more or less of the bronchial type in other portions of the lung. Such is believed to have been the real condition in Case 33 of the series, which, in its clinical course, gave very strongly the impression of a frank, lobar pneumonia, yet on physical examination and roentgenologically has to be grouped as a confluent bronchopneumonia.

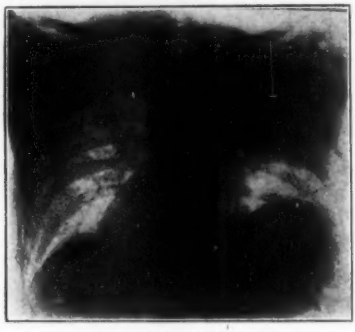

FIG. 4.—Illustrating lobar pneumonia.

Following is the descriptive postmortem pathology based on the report of Dr. Jean Oliver, who performed the autopsies in these cases as part of a series of 103.

The cases of lobar pneumonia differed in no way from the text-book description.

The few cases of acute interstitial pneumonia (McCallum) and of bronchopneumonia of the text-book variety seen at autopsy included no cases of this series.

On the other hand the postmortem pathology corresponding to the antemortem descriptive term "confluent" was nearly constant, and has been called "hemorrhagic bronchopneumonia," "hemorrhagic necrotizing bronchopneumonia," or "hemorrhagic pneumonitis." As this was the type found at postmortem in nearly all the cases of our series, an abstract of the description is given as follows:

In the newer lesions the prevailing picture was one of intense hyperemia and edema. Bloody fluid poured out of the sectioned lung, which was firm and doughy, especially posteriorly. At this stage there was little or no true consolidation.

Later a process of consolidation is added. Even the consolidated area is still very moist and indefinite. It runs in irregular bands through the lung tissue, leaving edematous areas still containing

air, the cut surface presenting a yellowish-gray appearance, streaked with the red or almost black hemorrhage of the earlier stage. Brownish-yellow pus now exudes from the lung tissue. There may be isolated areas of sharper outline and firmer consistency, which are really infarctions. Later still these isolated areas especially tend to undergo necrosis or the formation of abscesses from 1 to 5 cm. in diameter.

The bronchi are filled with pus, the mucous membrane undergoing destruction. The trachea is not usually involved except for hyperemia. The peribronchial lymph nodes are swollen, hemorrhagic or may contain abscesses.

The pleura is at first smooth and glistening, with more or less hemorrhage. Following this an exudation of fibrin occurs and in some cases a thin brownish-yellow pus develops.

Microscopically the infection is seen to originate chiefly in the smaller bronchi.

While the above description emphasizes the striking condition of hyperemia and edema, it should not be forgotten that practically all cases showed a considerable amount of consolidation or near-consolidation, especially in the posterior portions of the lungs, that could usually be detected clinically as areas of increased density.

The character of the lesion was liable to declare itself early. Except for the more intensive "diffuse" cases, already referred to as borderline, there was little or no tendency of lesser lesions to become transformed into the graver type. It is plain that on the accuracy of this statement depends very largely the value of the others. In its support are offered the consecutive physical and roentgen-ray examinations made in individual cases, especially the radiographic evidence.

On the basis of physical examinations and in most cases roentgen ray reports of the 67 cases were distributed as follows:

TABLE I

	Cases.	Deaths.
Bronchopneumonia:		
Discreet	15	0
Diffuse	19	2
Confluent	15	13
Lobar pneumonia	12	1
Negative as to pneumonia	6	0
Total	67	16

There was a total of 16 deaths, or 26 per cent. mortality, in the pneumonia cases. Of the 16 deaths 13 were recognized clinically as confluent; 2 were regarded as diffuse, but were in reality confluent by the time they came to autopsy at least. One was lobar pneumonia complicated by empyema and peritonitis. No discreet case died. Thus it is seen it was the exception for any confluent case to get well and the exception for any other type to die.

TEMPERATURE, PULSE AND RESPIRATION. Next to the determination of the confluent type of bronchopneumonia a rapid respiratory rate (with cyanosis) in the presence of bronchopneumonia was a particularly ominous sign (Table II). Taking as a standard a respiratory rate of 40 or over, maintained for two days or more, 10 of the confluent cases had such a respiration, with 9 deaths. The 2 diffuse cases which died also breathed in this way. Altogether there were 17 in this class, with only 5 recoveries, and 3 of the recoveries were patients with lobar pneumonia. The respiratory rate did not, therefore, seem to have the same significance in lobar pneumonia as it had in bronchopneumonia.

TABLE II

Respiration over 40:	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Fatal	0	2	9	1	0	12
Non-fatal	0	1	1	3	0	5
Respiration 40 or under:						
Fatal	0	0	4	0	0	4
Non-fatal	15	16	1	8	6	46
Total	15	19	15	12	6	67

The temperature (Table III) furnished no prognostic indications comparable with the respiration, nor did the pulse. Thirty-four cases ran a temperature over 104°, and of the 11 deaths in this class 9 were of the confluent type.

TABLE III

Temp. over.	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
104°—Fatal	0	1	9	1	0	11
Non-fatal	7	5	2	6	3	23
103°—Fatal	0	1	4	0	0	5
Non-fatal	6	7	0	5	1	19
102°—Fatal	0	0	0	0	0	0
Non-fatal	2	3	0	0	1	6
101°—Fatal	0	0	0	0	0	0
Non-fatal	0	2	0	0	1	3
Total	15	19	15	12	6	67

Of the 16 cases that died only 8 had a pulse-rate over 120, at least not until moribund. A pulse slow in proportion to temperature was generally seen and postfebrile bradycardia was pronounced in 15 cases.

TABLE IV

Chill:	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Fatal	0	1	3	1	0	5
Non-fatal	7	7	0	7	2	23
No chill:						
Fatal	0	1	5	0	0	6
Non-fatal	8	10	0	4	4	26
Total	15	19	8	12	6	60

CHILL AND HEMOPTYSIS. Positive or negative record of chill was made in 60 cases (Table IV). Twenty-eight cases had chill; 32 had not. The mortality in the former was 18 per cent. In the latter 23 per cent., a difference of no significance.

With regard to hemoptysis the record (Table V) showed 27 positive with 30 per cent. deaths, and 35 negative with a death-rate of 11.5 per cent. The difference here seems great enough to be regarded, especially when it is noted that in the group not showing hemoptysis none died except the confluent type. At the same time either cyanosis, abdominal distention or jaundice was regarded a graver sign than hemoptysis.

TABLE V

	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Hemoptysis:						
Fatal	0	2	5	1	0	8
Non-fatal	5	8	1	5	0	19
No hemoptysis:						
Fatal	0	0	4	0	0	4
Non-fatal	10	9	0	6	6	31
Total	15	19	10	12	6	62

SPUTUM BACTERIOLOGY. Using the Avery method the sputum was examined in 52 cases (Table VI).

TABLE VI

Pneumococcus:	Cases.	Fatal.
Type I	3	0
Type III	1	0
Type IV	26	6
Types I and II	1	1
Type II and hemolytic streptococcus	1	0
Type IV and hemolytic streptococcus	1	1
Type IV and non-hemolytic streptococcus	2	0
Type IV and undetermined streptococcus	1	1
Hemolytic streptococcus	4	2
Non-hemolytic streptococcus	11	1
Non-hemolytic streptococcus and Bacillus influenzæ	1	0
	52	12

The Bacillus influenzæ was demonstrated only once and then in combination with a streptococcus. The results in all other cases were a pneumococcus or streptococcus or a combination of both. The sputum bacteriology had to be considered of little or no prognostic value, for in the first place it had no relation to the type of pneumonia (Table VII).

Streptococci alone were found in the sputum of lobar cases, and pneumococci (chiefly Type IV, it is true) were found alone in many of the bronchial type. This is not to say whether or not the streptococcus can produce a true lobar pneumonia. It does make questionable the value of such sputum examinations under the conditions being discussed.

TABLE VII

Pneumococcus:	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Type I	0	1	0	2	0	3
Type III	0	0	0	1	0	1
Type IV	8	5	6	3	3	25
Types I and II	0	0	0	1	0	1
Type II and hemolytic streptococcus	0	0	1	0	0	1
Type IV and hemolytic streptococcus	0	0	1	0	0	1
Type IV and non-hemolytic streptococcus	1	1	0	0	0	2
Type IV and undetermined streptococcus	0	0	1	0	0	1
Hemolytic streptococcus	2	0	1	0	1	4
Non-hemolytic streptococcus	2	5	1	3	0	11
Non-hemolytic streptococcus and Bacillus influenzæ	0	0	0	1	0	1
Undetermined streptococcus and tubercle bacilli	0	0	1	0	0	1
Non-hemolytic streptococcus and tubercle bacilli	0	1	0	0	0	1
Total	13	13	12	11	4	53

The fact that in these cases the organism reported as predominating in the sputum bore no relation to the type of pneumonia is clearly indicated by Chart I. The curves for pneumococci and for streptococci alone or in association with other organisms correspond very closely to the base line indicating the relative incidence of the different types of pneumonia.

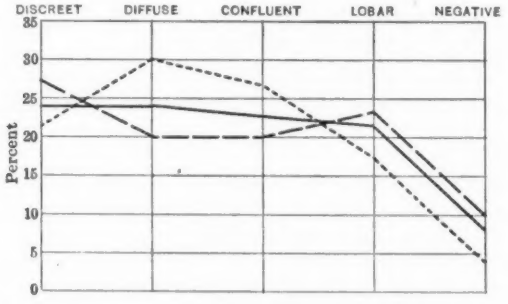

CHART I.—Base line ———, 53 cases. Pneumococci alone — — —, 30 cases. Streptococci alone (15 cases) and with pneumococci (5 cases) or other organisms (3 cases) ------.

Again (Table VIII) in each case cultured at postmortem (12 cases) a streptococcus was recovered from the lung tissue, a Strepto-

coccus hemolyticus nine times, whereas it had been found in the sputum of only 2 of these 9 cases. It should be stated, however, that in 3 of these 9 cases the sputum had not been examined.

TABLE VIII

Case No.	Sputum bacteriology.	Lung bacteriology at autopsy.
2	Pneumococcus, Type IV; streptococcus undetermined	Non-hemolytic streptococcus.
3	.....	Hemolytic streptococcus.
4	Pneumococcus, Type IV	Hemolytic streptococcus.
5	.....	Pneumococcus, Type IV; hemolytic streptococcus.
7	Pneumococcus, Type IV; hemolytic streptococcus	Hemolytic streptococcus.
15	.....	Non-hemolytic streptococcus (same in antemortem blood).
16	Non-hemolytic streptococcus	
21	Hemolytic streptococcus	Hemolytic streptococcus.
25	Bacillus tuberculosis	
29	Pneumococcus, Type IV	Hemolytic streptococcus (undedetermined streptococcus in antemortem pleural fluid).
47	.....	Hemolytic streptococcus.
53	Pneumococcus, Types I and II	Hemolytic streptococcus.
60	Pneumococcus, Type IV	
61	Pneumococcus, Type IV	Non-hemolytic streptococcus; Bacillus influenzæ.
62	Pneumococcus, Type IV	Hemolytic streptococcus.
63	Pneumococcus, Type IV	

Blood Cultures. Blood cultures were made in 54 cases, of which only 3 were positive. Each of these gave a non-hemolytic streptococcus. Two had been diagnosticated diffuse bronchopneumonia and one lobar pneumonia. One of the so-called diffuse cases (really confluent) died, the other and the case regarded as lobar pneumonia got well. The blood cultures and sputum ran truer to each other than did the postmortem lung bacteriology and sputum. Of the three non-hemolytic streptococcic blood cultures two had shown the same organism in the sputum, while in the third the sputum was not examined. With so small a percentage of positive blood cultures manifestly this procedure was of no value in prognosis. A larger number of positive results might have been obtained if repeated attempts had been made in individual cases. More than one culture was made in only a few cases.

Blood Counts. Blood counts were made in 62 cases (Table IX). A count under 10,000 was obtained in 45 cases, with 12 deaths, (27 per cent.), and a count above normal in 17 cases with 3 deaths (18 per cent.). A leukocytosis did not point to recovery when it occurred in the confluent type and a low or normal count was not often of bad prognostic import in other types.

Blood-pressures. Blood-pressures were recorded in 55 cases (Chart II). On the basis of a single reading taken at the height of illness the systolic pressure was slightly higher in the fatal cases

than in the non-fatal, the systolic relatively higher than the diastolic, giving a slightly wider pulse-pressure in the fatal cases, an average

TABLE IX

	Disc.	Diff.	Conf.	Lobar.	Neg.	Total.
Under 5000:						
Fatal	0	0	0	0	0	0
Non-fatal	2	3	0	1	0	6
5000 to 10,000:						
Fatal	0	2	9	1	0	12
Non-fatal	10	9	1	3	4	27
10,000 to 15,000:						
Fatal	0	0	1	0	0	1
Non-fatal	0	2	0	3	1	6
Over 15,000:						
Fatal	0	0	2	0	0	2
Non-fatal	3	1	1	3	0	8
Total	15	17	14	11	5	62

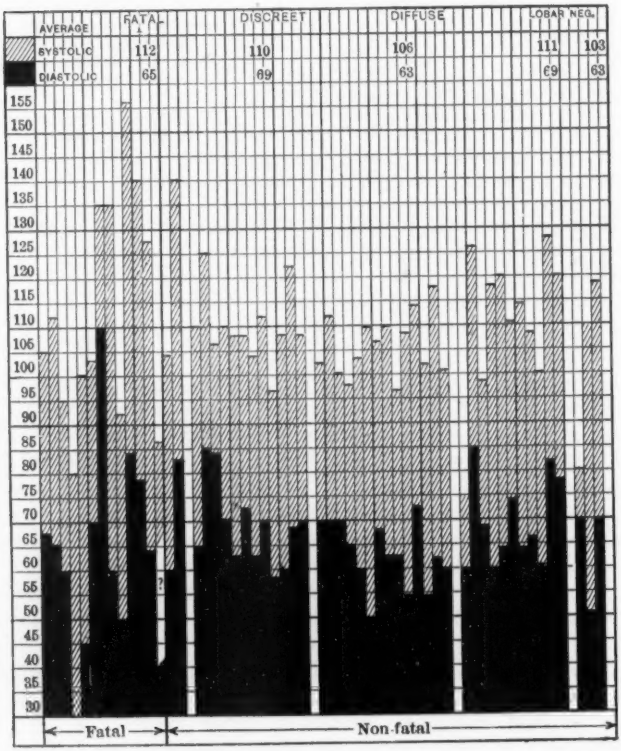

CHART II

of 47 as against 40 to 43 in the different types of non-fatal cases. There was less uniformity in the readings of the fatal group. There were no differences of value in prognosis. In general the averages were slightly lower than normal for men between the ages of twenty-one and thirty-one years.

In 8 non-fatal cases in which subsequent readings were recorded during convalescence there was an average systolic gain of twelve points, and an average diastolic gain of fifteen points. In 4 fatal cases in which subsequent readings were recorded before death they also showed an average gain of seven points systolic and nineteen points diastolic. No explanation of this unexpected finding is attempted.

TABLE X

	Fatal.	Non-fatal.
Empyema and meningismus in bronchopneumonia	Case 26	
Empyema in bronchopneumonia and pulmonary tuberculosis	" 23	Case 29
Empyema and peritonitis in lobar pneumonia	" 50	
Empyema in lobar pneumonia	" 50	" 6
Primary diarrhea and gross urinary findings	" 44	
Septicemia (non-hemolytic streptococcus)	" 15	Cases 18, 21
Membranous tonsillitis, purulent conjunctivitis and ulcerated foreskin		Case 1
Follicular tonsillitis		" 10
Otitis media		" 12
Primary dysentery		" 13
Abscess cellular tissue of back		" 62
Ischiorectal abscess		" 33
Syphilis		" 22
Recrudescence		" 45

COMPLICATIONS. The most frequent complications were empyema and pulmonary tuberculosis (Table X). In 2 cases only was the complication believed to be an important factor in the fatal termination, 1 of bronchopneumonia complicated by pulmonary tuberculosis and empyema, and 1 of lobar pneumonia, with a late complicating empyema and peritonitis. Subcutaneous emphysema was seen four or five times in the cases admitted to the hospital during the period under discussion, but did not occur in the series here included. Unusually gross urinary findings were reported in one case only of the series. This case died, but the kidneys were reported not grossly diseased at autopsy.

In the matter of race no differences in mortality were noticeable between white and colored troops. Deaths were about proportionate to incidence in the two races. The patients were all males, and age does not enter as a factor, as the men were all between the ages of twenty-one and thirty-one years.

It would be natural to inquire whether treatment did not play a part in the prognosis of these cases. Conditions of exposure and bodily exertion prior to entrance into a Base Hospital; distance of transportation and similar factors were, no doubt, highly significant.

After reaching the Base Hospital, from which the patient need not be evacuated until his condition warranted, the treatment carried out was essentially the same in all cases, being almost entirely symptomatic except for operations for empyema.

SUMMARY. It is desired to emphasize certain simple bedside standards of prognosis because the other data seem to be less significant as to the outcome in a given case.

The fatal type of pneumonia occurring in this series as seen at autopsy was that to which the name hemorrhagic bronchopneumonia or hemorrhagic pneumonitis has been applied.

This type could usually be recognized clinically as a confluent bronchopneumonia, bilateral, with evidence of considerable consolidation, yet the consolidation not of a frank lobar type. It was usually characterized by a respiratory rate of forty or over for a period of two days or more, and this rate was rarely seen in bronchopneumonia of other grades. Cyanosis was usually proportionate to the respiratory rate.

In lobar pneumonia a rapid respiratory rate was not so significant.

The roentgen ray was of great assistance in locating and defining small areas of pneumonia, in determining the presence or absence of fluid and other complications, but it was usually not essential to the diagnosis of the confluent type.

In conclusion, the data presented may be summarized in a very simple statement. Having recognized the existence of a bronchial type of pneumonia as distinguished from a lobar type, the question of prognosis seemed to be largely a matter of the density and extent of the pulmonary lesions.

My thanks are due Dr. Fred M. Hodges for the roentgen-ray studies and Dr. E. Guy Hopkins for the clinical laboratory data.[1]

THE TREATMENT OF ACUTE GONORRHEA IN FEMALES.

BY FRANK BENTON BLOCK, M.D., F.A.C.S.,

PHILADELPHIA, PA.

(From the Department of Gynecology, University of Pennsylvania School of Medicine.)

IN the very beginning of this paper it is my desire to state that I have no new method of treatment to offer, I have not discovered a "sure cure" for gonorrhea and I have no criticism to make of the many methods of treatment now in vogue. However, a close relationship with undergraduate medical students for several years has

[1] The detailed clinical data and abstracts of the physical, roentgen-ray and postmortem findings of the cases forming the basis of this report were submitted for publication, but have been omitted because of lack of space.—ED.

brought to my attention that there is something lacking in the present teachings on the subject of acute gonorrhea, and as nearly as I can determine the lacking element is the failure on the part of medical schools and medical authors to tell the student exactly what to do and to show him how to do it. The student attends lectures and clinics by the score, but almost invariably the subjects considered are operative conditions and technic, and it is only in very rare instances that much time is spent in discussing local treatment. Even more important is the very small opportunity that is presented to the average student to see how local treatments are applied and to actually apply them himself. It has often been truthfully stated by students that they graduate from medical schools prepared to perform a hysterectomy while they do not know how to insert a speculum into the vagina. They add little to their knowledge, as a rule, during their service as interns, and, as a result, when they take up active practise they are very poorly qualified to treat the so-called non-operative gynecological cases. An attempt has been made to overcome this state of affairs in the gynecological department of the University of Pennsylvania Medical School by giving the students practical work in the dispensary for a period of ten weeks. The course has been greatly appreciated by practically all of the students who have taken it, but in order to make it a real benefit it has been necessary to limit the classes to a few men at a time, so that only about 10 per cent. of the students have an opportunity of taking the course.

To the student or practitioner who consults such an excellent monograph as that of Norris[1] there will be ample opportunity to obtain a complete *résumé* of all that we know about the treatment of gonorrhea, and one or two of the more recent text-books contain excellent articles on this subject; but the general tendency of authors has been to lightly skip over the acute stage of the disease and then dilate upon the chronic stage and its complications. This appears especially ludicrous in view of the fact that careful observation and treatment during the acute stage may frequently prevent the ravages of pelvic inflammatory disease. At this point I should like to mention the wrong impression that is held by the average practitioner, due, no doubt, to erroneous instruction during student days, namely, that gonorrhea in the female is an incurable disease. In large measure this view is probably the result of Noeggerath's dictum, "Once infected, always infected," but such a statement does not hold good so long as the infecting organism has not passed into the uterine canal above the internal os. It is a common experience for the gynecologist to cure cases of acute endocervicitis, and yet the physician in general practice is always skeptical about such a report. The object of this paper, therefore, is to encourage more

[1] Gonorrhea in Women, Philadelphia and London, 1913.

extensive instruction in the treatment of acute gonorrhea in the female, so that the practitioner may undertake the treatment of these cases with a cheerful optimism as to the outcome, even though he may not be successful in all cases. In describing the method of treatment that has given me the most satisfaction, I shall divide the subject into acute urethritis and acute endocervicitis, since these are the most common types of infection. Acute inflammation of the vulvovaginal glands will not be considered, as it is freely admitted that it is my belief that we are unable to cure this condition without extirpating the glands, and any cases of non-operative cure that have occurred are, to my mind, not the result of any special line of treatment.

Acute Urethritis. Acute urethritis, which is usually the first stage of acute gonorrhea, is best treated by absolute rest and no local treatment during the period of the acute purulent discharge. The average patient who suffers from this condition, however, cannot or will not remain in bed, so that we are obliged to treat them as ambulatory cases. At the dispensary of the University Hospital we give these patients two prescriptions, one for santal oil, which is taken in 10-minim doses, three times daily, and the other prescription is for a urinary sedative containing 5-minims of tincture of hyoscyamus and 10 grains of sodium bromide to 1 dram of the liquor of potassium citrate, which is taken every three hours. The patient is instructed to drink water freely and return in a week, at which time, if the acute inflammation persists, the treatment is continued in the same manner. In the course of two or three weeks most cases will show a marked improvement, as evidenced by the freedom from symptoms and the diminution or the disappearance of the urethral discharge. It is at this time and not until then that local treatment is instituted, and when the treatment is begun, the patient must be warned that freedom from symptoms does not mean freedom from disease, as there is a great temptation for the patient to discontinue treatment. We have tried many agents in the local treatment of urethritis, but have come back to the use of silver preparations, using either a 15 per cent. solution of silver nucleinate or a 5 per cent. solution of silver nitrate, which is applied to the entire length of the urethra by means of a small cotton swab on a nasal applicator. A word or two regarding details may not be amiss at this point, since close observance of the finer points in technic will determine the efficacy of the treatment.

The patient should urinate just before the treatment and then the urethra should be well dried by gently passing a dry wisp of cotton on an applicator into the urethra. This drying is important, because the power of any gonococcidal agent is enormously enhanced by previous drying of the parts. The medicament is then absorbed on another cotton swab and the entire urethra is painted by means of a slow spiral movement of the applicator, which is continued until

the bladder is reached. The applicator is then withdrawn by the same spiral motion, *in the same direction*, so that the cotton is being tightened on the applicator instead of being loosened. Failure to observe this small point may result in the unpleasant accident of having the cotton caught by the internal sphincter and retained in the bladder. Although this is disconcerting to the physician it need cause no alarm, as the patient will not be aware of its presence, and, moreover, she will pass it at a subsequent urination. These treatments are given every two or three days until improvement in the local condition is noticed, and then the frequency of the treatments is gradually reduced until all signs have disappeared. At this time smears should be taken, and after three successive negative smears have been obtained a cure may be assumed.

Acute Endocervicitis. In considering the treatment of gonorrheal endocervicitis we should not expect quite as rapid improvement as can be obtained in the treatment of urethritis; nevertheless, by conscientious and continued treatment we shall be rewarded by results far above the expectations of the average practitioner. As soon as we have determined the presence of a gonorrheal discharge from the cervix, we order hot douches of 1 to 8000 potassium permanganate solution to be taken four or five times daily. We have found this solution to have the best cleansing effect in these cases, and if ordinary care is used, many of the objectionable features of permanganate can be obviated. We order it for our patients in the form of 1-grain tablets, which are dissolved just before use. As soon as the discharge is well under control, which ordinarily occurs in about two weeks, we begin to give the patient local treatments to the cervical canal. In applying any medicated solution to the cervical canal one of the most important points that must be observed is that the canal should be thoroughly cleansed and dried in order that the medication may come into actual contact with the infecting organisms which lie in the cervical glands. It is utterly impossible for any drug to accomplish this in the presence of a thick discharge, or even the usual cervical plug of mucus, which effectively protects the underlying organisms from the action of any antiseptic. Therefore, in order to get the best results, it has been our practice to expose the cervix by means of a bivalve speculum, wipe away the major portion of the discharge and then thoroughly spray the cervix with an alkaline solution, in order to dissolve the mucus. The cervix is again dried and then an applicator soaked in an alkaline solution (liquor antisepticus alkalinus) is passed into the canal as far as the internal os and moved to and fro, after which a dry cotton swab is passed into the canal and the thin discharge removed. This process is repeated several times until all of the mucus is removed and the canal is left clean and dry. We are then ready to apply our medication, which may be any one of the usual gonococcides. Our own preference is for a 10 or 12.5 per cent. solution of silver nitrate, which is vigorously applied to the canal

as far as the internal os, and immediately afterward tincture of iodin is similarly applied. These two drugs form a fresh silver iodide in the cervical canal, as can be seen by the characteristic yellow color that is produced. Not infrequently the patient will complain of some lower abdominal cramps as soon as the tincture of iodin is applied. This is merely a uterine colic, due to the stimulation of the muscle produced by the iodin fumes, and need cause no alarm, as it will disappear in a minute or two. Following this application the cervix and cul-de-sac are thoroughly dried and the speculum withdrawn. Only in very exceptional cases is a tampon inserted.

The patient continues her douches at home and reports to the office for treatment two or three times a week for the first three weeks, after which time the condition is usually so improved that douches can be discontinued and the interval between treatments can be lengthened. When the discharge has lost all of its purulent character and has become scanty, smears should be taken, and after three negative smears, one of which should be taken just after a menstrual period, the patient may be discharged.

Such is the technic that has given us more than satisfactory results, but it is only by a careful observance of details that results will be obtained, and at times the successful execution of a treatment is a trying ordeal for the physician. Any practitioner who would undertake to treat these cases should bear in mind two important points: In the first place, any particular treatment takes time, especially in the beginning of the disease, when the discharge is profuse and it is practically impossible to follow this technic closely in less time than fifteen minutes, which is more time than many practitioners are accustomed to spend upon these cases. In the second place the treatment should be as free from pain as possible, because if the patient is not comfortable she will not remain quiet upon the table, it will be impossible to get good exposure of the parts, and without good exposure the treatment cannot be properly administered. This point is also of special importance in the beginning of the disease, when the vulva is so tender as a result of the irritating discharge that the slightest pressure causes pain, while the insertion of a speculum seems to be out of the question. In these cases I do not hesitate to use a local anesthetic, which is applied on a pledget of cotton to the vaginal outlet. By this means, together with a little encouragement to the patient, I have never had to abandon a treatment on account of pain; indeed, I have been successful in introducing a speculum in several cases after futile as well as painful attempts have been made by colleagues.

As was stated in the beginning of this paper, nothing new is presented in the field of therapeusis, but if the practitioner will follow the technic above outlined and follow it in detail, I feel sure that he will be rewarded by results that will change his opinion relative to the gloomy prognosis of this disease.

A STUDY OF SUGAR MOBILIZATION BASED UPON 228 HUMAN CASES.[1]

By G. L. Rohdenburg, M.D., A. Bernhard, B.S.,
AND
Otto Krehbiel, M.D.,
NEW YORK.

(From the Laboratory of the Lenox Hill Hospital, New York City.)

The advent of microchemical methods in blood chemistry has opened many new fields for investigation, one of these being the metabolism of sugar. Our present knowledge of sugar metabolism, based solely upon chemical examination of the blood, may be summarized in a brief statement: The normal sugar content of the blood varies between 60 and 120 mg. per 100 c.c.,[2] and when the concentration of blood sugar rises above 180 mg. per 100 c.c. then sugar usually appears in the urine.[3]

Jacobsen,[4] who determined the amount of blood sugar present before and at different periods after the administration of relatively large amounts of glucose, found that after the administration of glucose there was a sharp rise in the percentage of blood sugar, which attained its maximum in about one hour and then slowly receded, returning to normal within two hours after the ingestion of the sugar. Other investigators,[5] by employing slight modifications of Jacobsen's method, have arrived at similar conclusions.

The results of these investigations of sugar tolerance, as they are called, have usually been presented in the form of a curve. These curves have been plotted for varying time intervals; thus, some observers, have examined the blood every fifteen minutes, while others, in order to determine the duration of the reaction, have continued observation for four, five and six hours.

In the present investigation, metabolism of sugar has been viewed as a functional test and not as a study of metabolism. This attitude having been adopted, rigid standards must be laid down for the technic of the test itself and for the manner in which the resulting

[1] The clinical observations recorded in this paper were made in greater part at the Lenox Hill Hospital and the Lincoln Hospital. Through the courtesy of Drs. Semken, Jessup, Fitch and Grant, forty-six cases were examined by them in the wards and in the laboratory of the New York Skin and Cancer Hospital. Their results were kindly given us for inclusion in this paper. We beg to express our thanks and appreciation to them and to those others who have so generously provided us with clinical material.

[2] Williams and Humphreys: Arch. Int. Med., 1919, xxiii, 537.

[3] Hamman and Hirschman: Arch. Int. Med., 1917, xx, 761.

[4] Biochem. Ztschr., 1913, lvi, 471.

[5] Hopkins: Am. Jour. Med. Sc., 1915, cxlix, 254. Taylor and Hutton, Jr.: Biol. Chem., 1916, xxv, 173. Janney and Isaacson: Arch. Int. Med., 1918, xxii, 160.

data are presented. A functional test presupposes that under the influence of a given definite stimulus the organism in a definite time period reacts in a definite manner. All extrinsic conditions must be constant, so that all variations can definitely be ascribed to differences in the individual.

The technic of the test as applied to patients in the wards of the various hospitals was as follows: After an all-night fast the individual was given 100 gm. of anhydrous glucose dissolved in 300 c.c. of weak tea. Both blood and urinary specimens were obtained just before giving the glucose and again 45 and 120 minutes thereafter. The chemical examinations of the blood were made after the Meyers-Bailey[6] modification of the Lewis-Benedict[7] method. The urinary specimens were examined according to the quantitative method described by Benedict.

We are aware that curves constructed on sugar values obtained at different time intervals than those chosen, would more accurately establish the point of maximum sugar concentration in the blood and that our method of glucose administration may be open to dispute. However, the point of maximum sugar concentration is not of importance from our standpoint, and varying the amount of glucose given according to the body weight (method of Janney and Isaacson), alters the burden placed on the organism. Variations of this character are not made in other functional tests. Thus with phenolsulphonephthalein the amount of dye injected is not changed to conform to the age, weight or other condition of the individual to be tested.

The investigations recorded in the succeeding paragraphs were prompted by the results recorded in another publication.[8] It was distinctly stated in that report that it was a preliminary one and it was emphasized that no definite conclusions were drawn. Our results as incorporated in that article, using the time intervals as given in this paper, seemed to indicate, on the basis of the material available, that there was a type of reaction peculiar to cancer.

The data collected as a result of the examinations recorded here will be considered under two heads: (*a*) statistical, and (*b*) pathological condition present.

Following the method outlined, three different types of reaction were encountered. The three types closely follow those described by McCasky.[9] In the type arbitrarily termed 1 the blood sugar at the 45 minute interval rises above the zero hour figure, and at the 120 minute interval is as high as or higher than at the 45 minute interval. In the type classed as 2 the rise at the 45 minute interval occurs as in type 1, but at the 120 minute interval the amount of

[6] Jour. Biol. Chem., 1916, xxiv, 147.
[7] Ibid., 1915, xx, 61.
[8] Rohdenburg, Bernhard and Krehbiel: Jour. Am. Med. Assn., 1919, lxxii, 1528.
[9] Jour. Am. Med. Assn., 1919, lxxiii, 245.

blood sugar has fallen more or less completely to the original figure. In the last type called 3 the initial sugar concentration is higher than or the same as that at 45 minutes, and the 120 minute interval shows a return to the original figures more or less complete, sometimes even going much higher.

If the pathological condition be completely disregarded and the cases be grouped solely according to the type of reaction found some interesting facts are demonstrable. The first 166 cases examined have been considered purely from this standpoint.

TABLE I.

	Type 1.	Type 2.	Type 3.
No sugar in urine . .	33 (50%)	49 (53%)	8 (100%)
Sugar in urine . . .	33 (50%)	43 (47%)	0
Total	66 (39%)	92 (55%)	8 (6%)

RENAL THRESHOLD OF THOSE SHOWING SUGAR.

		Mg. per 100 c.c.		Mg. per 100 c.c.		Mg. per 100 c.c.	
		Type 1.	Number.*	Type 2.	Number.*	Type 3.	Number.*
Zero .	High	212	4	212	1		
	Average	170	13%	212	4%	0	
	Low	126	..	212			
45 mins. .	High	304	16	400	30		
	Average	209	48%	188	69%	0	
	Low	135	..	141	..		
120 mins.	High	360	13	264	12		
	Average	226	39%	186	27%	0	
	Low	153	..	55	..		
NOT SHOWING SUGAR.							
Zero . .	High	198	..	138	..	212	
	Average	153	..	126	..	142	
	Low	45	..	55	..	106	
45 mins. .	High	265	..	280	..	192	
	Average	202	..	178	..	119	
	Low	72	..	100	..	83	
120 mins.	High	330	..	220	..	141	
	Average	292	..	139	..	60	
	Low	126	..	62	..	60	

* Indicates number of cases showing sugar in urine at this time interval.

The three types were represented (Table I) in the following proportions: type 1, 39 per cent.; type 2, 55 per cent.; type 3, 6 per cent. If each type in turn be considered from the standpoint of sugar elimination in the urine it will be noted that 50 per cent. of type 1 showed sugar at some period during the test as compared with 47 per cent. of type 2 and none of type 3. If each type be divided according to the excretion of sugar in the urine and the average concentration of blood sugar be compared in those excreting sugar and those not, it will be noted that the elimination of sugar

apparently bears but a slight relation to the concentration in the blood. Thus in type 1 in those showing sugar in the urine the average concentration of blood sugar at the various time periods was 170, 209, 226 mg., while in the same group those not showing sugar in the urine had as averages for the same periods 153, 202, 292 mg. In type 2 the figures for those showing sugar in the urine were 212, 188, 186 mg., while those showing no sugar had as averages 126, 178, 139 mg. Type 3 showed no sugar in the urine. In type 1, therefore, the average sugar concentration at the end of 120 minutes was higher in those showing no sugar in the urine than in those showing sugar, and this average was higher than the commonly accepted concentration of a normal renal threshold (180 mg.). Type 2, on the other hand, the figures for the zero hour being disregarded, since but one case showed sugar at that period, follows the commonly accepted standard. There is evidently some factor other than the mere concentration of sugar in the blood stream, which is responsible for the glycosuria.

The criticism may perhaps be made that because of the time intervals chosen the point of maximum sugar concentration in the blood was not ascertained; hence our deductions are faulty. If this criticism be true it applies with equal force to all groups and it does not explain why with one group of type 1 sugar should appear in the urine, with a concentration in the blood stream averaging 62 mg., less than in another group of the same type which did not excrete sugar.

The wide variation between maximum and minimum in any given group at any time interval would indicate that the actual determination of a point of maximum sugar concentration can have but little value in the diagnosis of pathological conditions, whatever may be its value from a metabolic standpoint. Varied as were the pathological conditions considered in our experiments it is interesting to note that in many of them the figures for the zero hour were distinctly higher than those currently accepted as normal.

An analysis correlated with the diagnosis of the patients examined is fully as interesting as the purely statistical review just made. In 228 cases reported here the diagnosis of all but 13 has either been confirmed by the pathological report (culture, section, or autopsy) or by the subsequent course of the case. The various pathological conditions encountered have been grouped, the reactions classified and the average figures given in Table II, while in Table III the data for each case are given individually.

In nephritis our results in agreement with those recorded by others show an initial hyperglycemia, with 75 per cent. of the cases giving a type 2 reaction.

In the two conditions pathologically classed as granulomata, in which the exciting cause is known—tuberculosis and syphilis—an initial hyperglycemia is not present, and while 60 per cent. of the

tuberculous cases show type 1 reaction, 72 per cent. of the syphilitics showed type 2. It is interesting to note that though the concentration of blood sugar was lower in tuberculosis than in syphilis, nevertheless a larger percentage of tuberculous cases excreted sugar. If concentration of the blood sugar were the only factor concerned in the excretion of sugar then the reverse should have occurred.

TABLE II.

Pathological condition.	No. of cases.	Mg. sugar per 100 c.c. blood.			Per cent. showing sugar in urine.	Per cent. of total number in this group.
		0 hr.	45 min.	120 min.		
			TYPE 1.			
Nephritis	2	170	233	294	50	25
Tuberculosis	4	97	156	198	50	60
Syphilis	2	77	178	205	0	28
Diabetes	4	139	310	390	100	37
Thrombo-angiitis obliterans	8	114	184	225	62	22
Pregnancy	2	141	169	188	50	66
Chorea	2	129	177	236	0	50
Exophthalmic goitre	2	123	211	238	100	50
Simple goitre	1	86	204	250	100	100
Pyogenic infections	3	119	165	169	0	30
Degenerative conditions	2	96	163	239	0	50
Benign tumors	4	136	204	252	50	31
Epithelioma	17	106	158	198	76	56
Carcinoma, stomach	11	111	191	219	27	61
Carcinoma, intestines	4	105	172	193	50	50
Carcinoma, breast	4	95	183	196	25	30
Carcinoma, genital organs	1	110	250	360	100	20
Malignant tumors not classified	10	111	192	225	30	66
			TYPE 2.			
Nephritis	6	131	217	153	50	75
Tuberculosis	3	91	188	100	38	30
Syphilis	5	97	177	120	20	72
Diabetes	5	162	319	269	100	63
Thrombo-angiitis obliterans	34	119	191	154	41	75
Pregnancy	1	126	204	152	100	33
Chorea	2	121	240	189	0	50
Exophthalmic goitre	2	105	122	118	50	50
Pyogenic infections	7	101	174	152	14	70
Degenerative conditions	2	97	160	114	50	50
Benign tumors	6	113	202	143	66	46
Epithelioma	13	95	174	126	46	44
Carcinoma, stomach	6	102	220	184	50	33
Carcinoma, intestines	4	137	233	162	25	50
Carcinoma, breast	8	111	186	144	37	61
Carcinoma, genital organs	4	125	208	156	0	80
Malignant tumors not classified	3	109	170	135	0	20
			TYPE 3.			
Tuberculosis	1	125	83	66	0	10
Thrombo-angiitis obliterans	1	106	106	106	0	3
Benign tumors	3	136	115	99	0	23
Carcinoma, stomach	2	118	105	156	50	6
Carcinoma, breast	1	117	100	95	0	9
Malignant tumors not classified	2	144	122	119	50	13

TABLE III.

Case No.	Disease.	Mg. sugar per 100 c.c. blood.			Urinary sugar.		
		0 hr.	45 min.	120 min.	0 hr.	45 min.	120 min.
16697	Tuberculosis	105	213	266	+	+	+
16762	"	100	107	111	+	−	−
L 79	"	100	200	260	−	−	−
L 89	"	112	210	50	−	−	−
L 460	"	45	72	157	−	+	−
487	"	125	83	66	−	−	−
1356	"	106	180	204	−	−	−
3836	"	72	204	114	−	−	−
4283	"	90	150	138	−	−	−
2726	"	128	168	192	−	−	−
4634	Syphilis	144	189	144	−	−	−
4239	"	117	245	147	−	−	−
1858	"	92	232	268	−	−	−
1337	"	96	232	180	−	−	−
L 86	"	65	115	75	−	−	−
440	"	66	105	55	−	−	−
J O B	"	62	125	142	−	−	−
P 502	Pregnancy	126	204	152	−	+	+
5708	"	136	156	186	+	+	+
3980	"	146	183	189	−	−	−
D 1210	Diabetes	144	312	304	−	+	+
2878	"	186	268	288	−	+	+
801	"	172	315	260	+	+	+
P 610	"	212	380	310	−	+	+
P 304	"	150	280	384	+	+	+
P 508	"	204	400	384	+	+	+
P 608	"	80	192	90	+	+	+
4046	"	81	384	500	−	+	+
D 210	Exophthalmic goitre	106	141	110	−	+	−
5809	" "	126	232	264	−	−	+
6570	" "	104	104	126	−	−	−
P 820	" "	120	190	212	−	+	+
1784	Simple goitre	86	204	250	−	−	+
3839	Chorea	122	208	232	−	−	−
3840	"	136	147	240	−	−	−
4242	"	114	216	138	−	−	−
4243	"	129	265	240	−	−	−
L 76	Nephritis	120	200	180	−	−	−
77	"	100	116	104	−	−	−
80	"	200	340	100	−	−	−
87	"	154	200	166	−	−	−
P 1	"	96	244	212	−	−	−
D 279	"	117	204	156	−	−	+
4363	"	168	265	348	+	+	+
2735	"	172	212	240	−	−	−
2916	Cholecystitis	135	144	144	−	−	−
3205	Fistula in ano	105	168	180	−	−	−
2633	Rheumatic fever	80	219	177	−	−	−
P 795	Endocarditis	118	184	189	−	−	−
4632	"	120	200	188	−	−	−
4404	Suppurative arthritis	126	189	184	−	+	+
3002	" "	96	138	126	−	−	−
2576	Lung abscess	106	190	188	−	−	−
16682	Cellulitis, neck	85	100	76	−	−	−
16662	Abscess, face	95	187	129	−	−	−
2349	Postoperative adhesions	96	192	165	−	−	−
1286	Chronic appendicitis	106	212	192	−	−	−

TABLE III—*continued.*

Case No.	Disease.	Mg. sugar per 100 c.c. blood.			Urinary sugar.		
		0 hr.	45 min.	120 min.	0 hr.	45 min.	120 min.
3138	Chronic appendicitis	117	240	285	−	−	+
P 145	Acromegaly	126	144	129	−	−	−
2585	Cretinism	126	132	82	−	−	−
D 286	Spondylitis	82	235	265	−	+	+
2562	Bronchial asthma	144	172	201	−	−	−
L 74	Cirrhosis of liver	100	200	320	−	−	−
L 83	" "	71	100	75	−	−	+
L 78	Apoplexy	124	220	154	−	−	−
3851	Myocarditis	92	126	159	−	−	−
S 1	Normal male	112	159	130	−	−	−
4447	Leukemia	159	204	160	−	−	−
129	Tobacco-poisoning	120	330	219	−	+	+
16724	Cystitic mastitis	175	266	210	−	+	−
D 358	Exostosis	78	152	111	−	−	−
D 186	"	147	228	134	−	+	+
3598	Fibromyoma uteri	212	322	336	−	+	+
408	" "	68	74	142	−	−	−
16640	" "	86	63	74	−	−	−
D 184	Foreign body	116	228	106	−	−	−
D 481	" "	57	95	76	−	−	+
P 146	Cyst adenoma of ovary	156	120	84	−	−	−
2066	" " "	198	265	320	−	−	−
453	Chronic inflammation	76	157	213	−	+	+
1304	Papilloma of bladder	106	245	225	−	−	+
2483	Congenital cystic kidney	168	164	141	−	−	−
16589	Epithelioma of penis	100	175	142	+	+	+
16620	" skin	86	199	249	+	+	+
16644	" cheek	100	117	175	−	+	+
16643	" lip	117	187	199	−	+	+
16440	" lip	153	229	260	−	+	+
16339	" cheek	133	166	133	−	−	+
16445	" larynx	142	142	229	−	−	+
16635	" larynx	117	213	175	+	+	+
16675	" lip	95	95	100	−	+	+
16744	" penis	100	160	214	−	−	−
16599	" lip	101	125	142	−	+	−
4245	" tongue	150	159	162	−	−	−
D 129	" buttock	166	236	180	−	−	+
3045	" larynx	129	192	192	−	+	+
S 16339	" cheek	64	187	105	−	−	−
S 16435	" face	99	142	153	−	−	+
H. S.	" lip	86	142	199	−	+	−
S 16378	" lip	105	160	125	−	−	−
1834	" cheek	122	228	144	−	−	−
2068	" cheek	80	244	265	−	−	−
1589	" esophagus	82	160	220	−	−	−
1691	" cheek	106	174	144	−	−	−
16357	" tongue	55	178	154	−	−	−
16450	" mouth	105	175	222	−	−	+
16439	" cheek	111	135	229	−	+	+
16368	" neck	100	166	105	−	+	+
16390	" nose	76	86	153	−	−	+
16436	" mouth	54	160	100	−	+	+
16404	" eyelid	55	122	62	−	−	+
16272	" face	57	100	62	−	−	−
2834	Carcinoma of stomach	116	168	230	−	−	−
2939	" "	78	215	210	−	−	−

TABLE III—*continued.*

Case No.	Disease.	Mg. sugar per 100 c.c. blood.			Urinary sugar.		
		0 hr.	45 min.	120 min.	0 hr.	45 min.	120 min.
1621	Carcinoma of stomach	106	275	245	−	−	+
2019	" "	110	183	183	−	−	+
2415	" "	76	212	212	−	−	−
859	" "	120	144	232	−	−	−
712	" "	108	228	288	−	+	+
974	" "	106	100	192	−	−	+
L 82	" "	100	240	220	−	+	+
L 90	" "	130	110	120	−	−	−
4648	" "	145	190	190	−	−	−
4174	" "	138	208	112	−	−	−
2429	" "	136	304	304	−	−	−
2096	" "	98	160	126	−	+	+
2708	" "	132	190	200	−	−	−
2794	" "	102	138	168	−	−	−
2946	" "	96	224	190	−	−	−
3353	" "	74	188	224	−	+	+
3728	" "	110	165	196	−	−	−
4079	" colon	120	240	156	−	−	+
4362	" colon	108	212	159	−	−	−
4352	" colon	174	265	185	−	−	−
S 16415	" cecum	116	200	216	−	+	−
1277	" sigmoid	55	129	157	−	−	+
7305	" rectum	123	158	189	−	−	−
2687	" rectum	126	205	240	−	−	−
D 718	" rectum	156	215	148	−	−	−
2001	" liver	123	189	184	−	−	−
4208	Hypernephroma of liver	126	212	212	−	−	+
2119	Carcinoma of pancreas	120	160	210	−	−	−
551	" pancreas	212	192	138	−	−	−
985	" pancreas	114	240	272	−	−	−
1895	" breast	86	232	236	−	+	+
P 2	" breast	138	183	117	−	−	−
P 3	" breast	126	162	150	−	+	+
2408	" breast	126	240	192	−	−	+
1456	" breast	96	180	180	−	−	−
L 75	" breast	100	250	170	−	−	−
L 84	" breast	144	180	150	−	−	−
L 85	" breast	100	166	120	−	−	−
L 88	" breast	80	146	114	−	−	−
S 16455	" breast	76	160	110	−	+	+
16406	" breast	117	100	95	−	−	−
2988	" breast	90	152	192	−	−	−
D 111	" breast	110	168	176	−	−	−
1979	" ovary	135	204	132	−	−	−
2512	Sarcoma of uterus	106	174	110	−	−	−
1043	Carcinoma of uterus	138	174	164	−	−	−
L 81	" uterus	120	280	220	−	−	−
S 16451	" uterus	110	250	360	−	−	+
L 98	Sarcoma of femur	98	170	220	−	−	−
2050	" kidney	90	132	76	−	−	−
16404	" orbit	101	187	199	−	−	+
2411	Carcinoma of lung	106	150	192	−	−	−
P 4	" lung	100	165	230	−	−	−
3056	" bladder	138	240	290	−	−	+
1436	" bladder	116	189	146	−	−	−
16673	" tonsil	76	63	100	−	+	+
16739	Metastatic carcinoma	120	199	213	−	+	+
5810	" "	96	204	215	−	−	−

TABLE III—*continued.*

Case No.	Disease.	Mg. sugar per 100 c.c. blood.			Urinary sugar.		
		0 hr.	45 min.	120 min.	0 hr.	45 min.	120 min.
W M 1	Thrombo-angiitis obliterans	106	138	216	−	−	+
2	" "	108	280	198	−	+	+
3	" "	168	192	126	−	+	+
4	" "	116	192	168	−	−	−
5	" "	106	116	96	−	−	−
6	" "	142	344	288	−	+	+
7	" "	210	300	280	−	+	+
8	" "	112	200	230	−	−	−
9	" "	124	180	159	−	−	−
10	" "	100	144	126	−	−	−
11	" "	96	159	116	−	−	−
12	" "	136	144	96	−	+	+
13	" "	129	265	240	−	+	+
14	" "	96	108	104	−	−	−
15	" "	126	164	96	−	−	−
16	" "	99	138	116	−	−	−
17	" "	116	184	174	−	−	−
18	" "	129	200	174	−	+	+
19	" "	116	162	129	−	+	+
20	" "	114	132	144	−	−	−
21	" "	100	162	120	−	+	+
22	" "	126	150	116	−	−	−
23	" "	120	129	106	−	−	−
24	" "	106	106	106	−	−	−
25	" "	96	320	192	−	+	+
26	" "	100	174	138	−	+	+
27	" "	116	159	116	−	−	−
28	" "	116	189	174	−	−	−
29	" "	102	198	198	−	−	−
30	" "	110	189	120	−	+	+
31	" "	106	189	159	−	−	−
32	" "	110	212	96	−	+	−
33	" "	100	174	100	−	−	−
34	" "	120	153	112	−	−	−
35	" "	116	150	190	−	−	−
36	" "	106	138	216	−	+	+
37	" "	108	280	198	−	+	+
38	" "	96	159	112	−	−	−
39	" "	153	240	208	−	+	+
40	" "	114	212	176	−	−	−
41	" "	156	252	350	−	+	+
42	" "	106	114	106	−	−	−
D 174	" "	100	265	280	−	+	+
	DIAGNOSIS OF FOLLOWING NOT PROVED						
D 42	Carcinoma of lung	100	208	196	−	−	−
2172	Brain tumor	176	240	264	+	+	+
1306	Ulcer of stomach	86	184	232	−	+	+
1390	" stomach	86	174	183	−	−	+
1624	Carcinoma of stomach	116	180	230	−	−	−
1603	" stomach	78	240	210	−	−	−
1674	" stomach	120	240	156	−	−	−
L 73	" stomach	120	200	160	−	−	−
2308	Gastroptosis	120	150	86	−	+	+
3055	"	156	176	168	−	+	+
7868	Neurasthenia	126	106	60	−	−	−
4369	"	96	114	123	−	−	−
861	Severe secondary anemia	108	152	144	−	−	−

The diabetics examined showed, as was to be expected, an initial hyperglycemia, with 60 per cent. of the cases giving a type 2 curve.

In the cases of thrombo-angiitis the initial figures were practically normal and the type of reaction in 75 per cent. of the cases was that of type 2.

In pregnancy there is also an initial hyperglycemia, and 66 per cent of the cases gave a type 1 reaction. Pyogenic infections gave 70 per cent. type 2 reaction.

In degenerative tissue conditions, such as cirrhosis of the liver, myocarditis, etc., one case was observed with a blood sugar concentration of 239 mg. without urinary leakage.

As we have stated before, our original paper had to do with the reaction in cases of cancer. Our present report necessitates a very considerable modification of our previous statements. In that paper we considered what we have since termed type 1 to be a possibly specific reaction in cancer.

In our series of benign tumors we have found 31 per cent. to give type 1 reaction as compared with 56 per cent. of epitheliomata, 61 per cent. of gastric carcinomata, 50 per cent. of intestinal carcinomata, 30 per cent. of breast carcinomata, 20 per cent. of genital organ carcinomata and 66 per cent. of other non-grouped malignant tumors. The actual number of cases is given in Table III. Initial hyperglycemia occurs in some instances, but is not constant. The fact that so high a percentage of type 1 reaction occurred with epitheliomata not showing cachexia renders untenable the theory that the high percentage given by gastric carcinomata is due to cachexia and the demand of the tissues for sugar.

CONCLUSIONS. It is evident, from the data here presented, that the organism may respond in one of three ways after the ingestion of 100 gm. of glucose. Neither of these three reaction types can be considered as diagnostic of any given pathological condition, though, in general, conditions associated with increased growth energy show a higher percentage of type 1 reaction. There is no fixed type of reaction even in metabolic disturbances, absolutely similar curves being found in conditions as widely different as diabetes, tuberculosis, epithelioma and pregnancy. Many diseased conditions are accompanied by hyperglycemia. The concentration of blood sugar is not the sole factor concerned in the development of glycosuria.

THE GERMICIDAL VALUE OF POTASSIUM MERCURIC IODIDE.

BY DOUGLAS MACFARLAN, M.D.,

SINCE the second year of the war the subject of antisepsis has acquired a new interest and need has arisen to refresh and revise

our knowledge of the relative merits and faults of various germicides. In former times personal preferences, based largely on empiricism, led to the choice of this or that chemical substance for the purpose of disinfecting operative sites and wounds. Oftentimes certain collateral qualities of the germicides, such as solubility, reputed lack of toxicity and so forth, rather than their actual killing power on bacteria under surgical conditions, were emphasized.

Any comparison of germicides should be based (1) on their bactericidal efficiency and (2) on their physical and chemical properties. For some time past the writer, realizing the disadvantages of many of the germicides in general use, has devoted himself to the study of potassium mercuric iodide.

Earlier experiments already reported[1] have demonstrated several marked advantages of this substance over other iodin and mercury salts in addition to its value in the treatment of infectious conditions,[2] [3] [4]. Watson[5] and Hinman[6] obtained fresh evidence of its high germicidal potency, while Rosenberger,[7] working with an analogous compound, confirmed the efficiency of this type of mercury salt.

Potassium mercuric iodide is a distinct chemical entity, formed by the direct combination of two molecules of potassium iodide with one molecule of mercuric iodide, and has the formula K_2HgI_4 or $HgI_2 2KI$. For this reaction, and also in order that the subsequent conversion of this double salt into the red iodide of mercury may be prevented, an excess of potassium iodide is necessary. In the crystalline state the salt is deliquescent, and upon taking up water, readily deposits the red mercuric iodide. It may, however, be obtained in tablet form, in which the two salts (mercuric iodide and potassium iodide) are bound by an inert soluble excipient and readily yield clear, stable solutions of the double salt. This is by far the most convenient form in which to obtain and employ this substance.

Before considering the high germicidal potency of potassium mercuric iodide four distinctive and valuable features making for its superiority over other salts of mercury and iodin may well be considered.

[1] Macfarlan, Douglas: Notes in the Study of Potassium Mercuric Iodide, Jour. Am. Med. Assn., January 3, 1914, lxii, 17–19.

[2] Macfarlan, Douglas: Still Another Suggestion for Atrophic Rhinitis; the Double Iodide of Mercury and Potassium, Jour. Ophthl., Otol. and Laryng., October, 1913, vol. xix.

[3] Macfarlan, Douglas: A Rationale of a New Treatment for the Acute Frontal Sinusitis, Jour. Ophth., Otol. and Laryng., September, 1915, vol. xxi.

[4] Macfarlan, Douglas: A Consideration of Pyorrhea and the Rationale of a New Remedy, with Case Reports, Jour. Ophth., Otol. and Laryng., November, 1916, vol. xxii.

[5] An Improved Substitute for Iodized Catgut Sutures, Surg., Gynec. and Obst., January, 1916, xxii, 114–115.

[6] Urinary Antiseptics, Jour. Am. Med. Assn., November 20, 1915, lxv, 1769.

[7] On Lithio Mercuric Iodide, Am. Med., June 25, 1904, vii, 1021.

1. *Solubility.* It is readily soluble in both water and alcohol as well as in acetone.

2. *Toxicity.* As compared with the most prominent metallic germicide—mercuric chloride—it is far less toxic, and, in dilutions effective for germicidal use, the factor of safety renders it comparatively harmless for irrigations of mucous membranes or for any purpose in which there is a likelihood of its being swallowed. Even a 1 per cent. solution may be taken internally in doses of six to eight drops without producing gastric irritability, while one would have to swallow about 30 c.c. of the 1 to 1000 solution or 300 c.c. of the 1 to 10,000 solution to obtain the maximum medicinal dose.

3. *Lack of Irritation.* One-half of 1 per cent. solutions are slightly irritating to the mucous membranes, causing a burning sensation with the stimulation of a watery secretion. Solutions of these strengths have little or no irritating effect on the skin when applied for twenty-four hours by a wet pack or compress, while dilutions of 1 to 1000 or more cause none of the disagreeable effects upon the hands produced by similar solutions of bichloride of mercury.

4. *Non-precipitation of Proteins.* Contrary to the action of other metallic germicides in the presence of proteins, potassium mercuric iodide fails to precipitate these substances. Experiments by the author have shown that so soluble is this salt in protein solutions that human blood serum readily dissolves 100 per cent. of potassium mercuric iodide without any appreciable coagulation or precipitation of the serum albumin or globulins. This lack of affinity for serum proteins is an important factor in those cases in which it is desired to achieve potent germicidal action in the presence of blood, pus or other tissues. That the germicidal action of the double salt, unlike other antiseptics and germicides, is only slightly diminished by the presence of organic matter will be shown in Table VII.

Germicidal Action. Potassium mercuric iodide has long been known as a potent germicide, exerting not only an antiseptic but a true killing power in high dilutions. In the well-known table of Park[8] the red iodide of mercury, the active component of the double salt, stands at the head of the list for potency. Earlier experiments by the author, reported in 1914,[1] showed that potassium mercuric iodide in a dilution of 1 to 80,000 killed such organisms as Bacillus typhosus, Staphylococcus aureus, Bacillus bulgaricus, Bacillus acidi lactici and a yeast after a twenty-four-hour exposure, while Watson,[5] comparing the action of the double iodide with that of iodin solutions, found that the former was far superior in its killing action on Staphylococci, Bacillus coli and even the sporulating Bacillus subtilis.

With a view to gaining additional and more exact information concerning the germicidal action of potassium mercuric iodide the

[8] Pathogenic Microörganisms, 6th ed., Philadelphia, Lea & Febiger, 1917, p. 668.

author, with the assistance of Dean, has carried out the following experiments:

1. *Technic.* A series of tubes containing the water solutions of potassium mercuric iodide of varying concentrations were inoculated with 0.1 c.c. of actively growing broth cultures of (1) Staphylococcus albus, (2) Bacillus coli communis and (3) Bacillus subtilis (containing free spores). At the end of the indicated exposures a 2 mm. loopful of the mixture was transferred to nutrient broth and the tubes incubated at 37.5°. Growth was further controlled by plating these incubated broth cultures.

2. *Results:*

TABLE I.—STAPHYLOCOCCUS ALBUS.

Dilution: K_2HgI_4.	Time of exposure (minutes). 3	5	10	20	30	60
1–5000	X	0	0	0	0	0
1–4000	0	0	0	0	0	0
1–3000	0	0	0	0	0	0
1–2000	0	0	0	0	0	0
1–1000	0	0	0	0	0	0
1– 500	0	0	0	0	0	0
1– 100	0	0	0	0	0	0
Broth control	X	X	X	X	X	X

X = Growth.
O = No growth

TABLE II.—STAPHYLOCOCCUS ALBUS (CONTINUED).

Dilution: K_2HgI_4.	Time of exposure (hours). ½	1	2	3	6	12	24
1–100,000	X	X	0	0	0	0	0
1– 90,000	X	X	0	0	0	0	0
1– 80,000	X	X	0	0	0	0	0
1– 70,000	X	X	0	0	0	0	0
1– 60,000	X	X	0	0	0	0	0
1– 50,000	X	X	0	0	0	0	0
1– 40,000	X	X	0	0	0	0	0
1– 30,000	X	X	0	0	0	0	0
1– 20,000	X	X	0	0	0	0	0
1– 10,000	X	X	0	0	0	0	0
Broth control	X	X	X	X	X	X	X

TABLE III.—BACILLUS COLI COMMUNIS.

Dilution: K_2HgI_4.	Time of exposure (minutes). 1	2	3	5	10	20	30	60
1–5000	X	X	X	X	X	X	X	0
1–4000	X	X	X	X	X	X	X	0
1–3000	X	X	X	X	X	0	0	0
1–2000	X	X	X	X	0	0	0	0
1–1000	X	X	0	0	0	0	0	0
1– 500	X	0	0	0	0	0	0	0
1– 100	0	0	0	0	0	0	0	0
Broth control	X	X	X	X	X	X	X	X

TABLE IV.—BACILLUS COLI COMMUNIS (CONTINUED).

Dilution: K_2HgI_4.	Time of exposure (hours). ½	1	2	3	4	5	6	12	24
1–100,000	X	X	X	X	X	X	X	X	X
1– 90,000	X	X	X	X	X	X	X	X	0
1– 80,000	X	X	X	X	X	X	X	X	0
1– 70,000	X	X	X	X	X	X	X	X	0
1– 60,000	X	X	X	X	X	X	X	X	0
1– 50,000	X	X	X	X	X	X	X	X	0
1– 40,000	X	X	X	X	X	X	X	0	0
1– 30,000	X	X	X	X	X	X	0	0	0
1– 20,000	X	X	X	0	0	0	0	0	0
1– 10,000	X	X	0	0	0	0	0	0	0
1– 5,000	X	0	0	0	0	0	0	0	0
1– 1,000	0	0	0	0	0	0	0	0	0
Broth control	X	X	X	X	X	X	X	X	X

TABLE V.—BACILLUS SUBTILIS.

Dilution: K_2HgI_4.	Time of exposure (minutes). 3	5	10	20	30	40	50	60
1–5000	X	X	X	X	X	X	X	X
	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
1–4000	X	X	X	X	X	X	X	X
1–3000	X	X	X	X	X	X	X	X
1–2000	X	X	X	X	X	X	X	X
1–1000	X	X	X	X	X	X	X	X
	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)
1– 500	X	X	X	X	X	X	X	0
	(X)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
1– 100	X	0	0	0	0	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Broth control	X	X	X	X	X	X	X	X

X = Growth, 0 = No growth } 1st series.

(X) = Growth, (0) = No growth } 2d series.

TABLE VI.—BACILLUS SUBTILIS (CONTINUED).

Dilution: K_2HgI_4.	Time of exposure (hours) ½	1	2	3	6	12	24
1–100,000	X	X	X	X	X	X	X
1– 90,000	..	..	..	..	..	..	X
1– 80,000	..	..	..	..	..	..	X
1– 70,000	..	..	..	..	..	..	X
1– 60,000	..	..	..	..	..	..	X
1– 50,000	X	X	X	X	X	X	X
1– 40,000	X	X	X	X	X	X	X
1– 30,000	X	X	X	X	X	X	X
1– 20,000	X	X	X	X	X	X	X
1– 10,000	X	X	X	X	X	X	0
	(X)	(X)	..	..	(X)		
1– 5,000	X	X	X	X	X	0	0
	(X)	(X)	..	..	(X)		
1– 1,000	X	X	X	X	0	0	0
	(X)	(X)					
Broth control	X	X	X	X	X	X	X

The above tables are self-explanatory. The results prove that potassium mercuric iodide possesses a remarkably high germicidal

efficiency. The fact that a pus-producing organism such as the Staphylococcus is killed in five minutes by a 1 to 5000 solution shows that this double iodide may be effectively used in dilutions which are incapable of producing irritation to the most sensitive tissues or of causing poisoning under the usual therapeutic conditions. In Tables V and VI the rapid action of 1 to 100 and even to 500 solutions on a sporulating culture of Bacillus subtilis may be taken as an indication of the action of this double salt on pathogenic sporulating bacilli such as the organisms of tetanus, anthrax, gas gangrene and malignant edema.

In order to determine to what extent the presence of organic matter, serum proteins especially, might interfere with or diminish the bactericidal action of potassium mercuric iodide, the following experiment was carried out:

I. *Technic.* To tubes containing 2 c.c. of the different dilutions of the germicide was added sufficient human serum to give an actual coagulable protein content of 0.5 per cent. (determined by gravimetric method). The solution remained perfectly clear, but solidified on boiling. The tubes were allowed to stand twenty-four hours to allow any possible reaction between the double iodide and the albumin to take place. The tubes were then inoculated with 0.1 c.c. of an actively growing broth culture of Staphylococcus albus freshly isolated from a human infection. After the stated period of exposure, subcultures, using one 2 mm. loopful, were made in liquefied nutrient agar at 40° and then plated. After incubation the plates showed either no growth or a heavy growth, except in the cases of the twelve-hour exposure, where the colonies were few.

II. *Results.*

TABLE VII.

Dilution, K_2HgI_4.	Staphylococcus, strain A.							Staphylococcus, strain B.							Staphylococcus, strain B, with human serum.						
	Time.							Time.							Time.						
	3″	5″	10″	30″	1′	6′	12′	3″	5″	10″	30″	1′	6′	12′	3″	5″	10″	30″	1′	6′	12′
1– 500 . .	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1– 1,000 . .	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1– 5,000 . .	X	0	0	0	0	0	0	0	0	0	0	0	0	0	X	X	X	X	0	0	0
1– 10,000 . .	X	X	X	X	0	0	0	X	X	X	X	X	0	0	X	X	X	X	X	0	0
1– 50,000 . .	X	X	X	X	X	0	0	X	X	X	X	X	X	X	X	X	X	X	X	X	X
1–100,000 . .	X	X	X	X	X	0	0	X	X	X	X	X	X	X	X	X	X	X	X	X	X

The results show that organic matter in the form of human serum albumin in a concentration of 0.5 per cent. has no appreciable effect on the germicidal action of 1 to 500 and 1 to 1000 solutions of potassium mercuric iodide. As might be expected with the weaker concentration of germicide, protein delays their bacterial action,

but this diminution is relatively slight when compared with McClintic's reports[9] on the germicidal powers of phenol and some commercial disinfectants in the presence of organic matter.

Discussion. The experiments submitted show that potassium mercuric iodide is a powerful germicide exhibiting marked bactericidal efficiency in high dilutions. Organic matter diminishes its potency to a relatively slight degree. These facts, taken in consideration with its great solubility, its freedom from irritant action and its comparatively low toxicity in the solutions efficacious for germicidal purposes, would seem to recommend this double salt of the iodides of potassium and mercury as the most desirable of the inorganic germicides.

[9] Hygienic Lab. Bull., April, 1912, lxxxii, 37 *et seq.*

ERRATA.

The Editor assumes responsibility for the unfortunate errors that occurred in the article entitled, "The Oculopupillary Fibers of the Sympathetic System: Division of the First Thoracic Root in Man," by William G. Spiller, M.D., which was published in the issue of this Journal for March, 1920, p. 325. Attention is called to the following corrections:

On page 326, line 39, a comma should be inserted after the word tactile.

On page 331, line 17, "Mmes. Dejerine and Klumpke" should be corrected to read "Madam Dejerine Klumpke."

On the same page, line 41, "She" should be changed to "He."

On line 44 of the same page, "Mmes. Dejerine and Klumpke" should again be corrected to "Madam Dejerine Klumpke."

On page 336, line 21, "her" should be changed to "his," and on line 24 of the same page, "she" should be changed to "he."

REVIEWS

LE TYPHUS EXANTHEMATIQUE. By D. DANIÉLOPOLU, M.D., Professeur Suppléant de Clinique médicale á la Faculté de Médecine de Bucarest. Médecin de l'hôpital Brancovan. Pp. 512; 87 illustrations and 6 plates in colors and monochrome. Bucarest: Charles Göbl, 1919.

ONE is accustomed to think of the Balkans as being in a continual state of unrest. From the accounts that we receive from this district we think only of the turmoil and excitement which seems to be continually present there. A good many of us have fixed in our minds the idea that no constructive work is being undertaken there; that the people are more or less existing only on the minimal amount of what in civil life is compatible with keeping body and soul together. Such an impression is distinctly obliterated when one sees a copy of the recent work of Dr. Daniélopolu, which has just come from Bucarest. This book is a splendidly gotten up volume and would do credit to any printer in a country which we consider more enlightened than Roumania. The quality of the paper is good, the printing is clear and without typographical errors, and the illustrations, for the most part, are clear-cut and well reproduced. But the astounding part of the book, at least to the reviewer, is the fact that Dr. Daniélopolu should be able to give the amount of study and work that he has done in this book on typhus fever during all the turbulence of the past war, when conditions were such that it did not seem possible for any physician to do more than the most routine medical work on account of the tremendous demands upon the medical man. The book is largely a volume of original observation, more particularly on the treatment of the disease, and his description of the symptomatology of the fever is a most careful clinical study.

During the war Dr. Daniélopolu had the opportunity to see and study a tremendous number of cases of typhus fever, and it is interesting to know the results of his study of these cases.

In regard to the etiology of the condition, he is didactic in his statement that it is a louse-born disease, and he quotes several reasons why he believes this, all of which are very positive and undoubted.

The louse which transmits the disease is the ordinary body louse, and Dr. Daniélopolu does not believe that the head louse is able to

transmit typhus. The incubation period is supposed to be from five to twenty-one days, but during the course of an epidemic the incubation becomes about equal for all cases, averaging from seven to eight days. Four cases are quoted to prove that the incubation period is of this length of time. For example a nurse on service in the typhus wards wore a special rubber costume; she went to the triage of the hospital without this special rubber costume, was bitten by a louse and seven days after developed the disease. Much the same history is given with three other cases. In the symptomatology of typhus fever the author, in addition to the clear-cut account of the usual symptoms, calls special attention to the unusual changes of the cerebrospinal fluid as made by the study of repeated punctures and which the author insists should be repeated many times on the individual cases. The fluid is of high tension, though never as high as in acute meningitis; it is usually clear, occasionally slightly cloudy and very frequently contains red blood cells, the result of cerebrospinal vasodilation and of effusions in the meninges. Occasionally there is a yellow discoloration which the author was the first to point out and which has been subsequently confirmed by others. Xanthochromia occurs in the cases showing more particularly nervous phenomena. It is necessary to examine the fluid immediately after withdrawal in order to demonstrate this phenomenon. There is also usually an increase in the cellular count of the spinal fluid, and the more severe the case, the higher the number of cells, which are especially increased when there is yellow fluid.

The leukocytes in the blood are much increased, and this increase is usually an absolute increase in all the cellular elements. There are numerous other valuable clinical observations: pulse tracings have been made, eye-ground examinations have been made and complete laboratory studies accomplished, and in every way the cases have been carefully worked up.

The latter part of the book is filled with case reports and details of the author's method of treatment, which consists essentially of the frequent intravenous injections of hypotonic salt solution, the percentage being sixty-five one-hundreds. The results of this treatment have been perfectly astounding. The percentage of the severe cases recovering, according to the special method that the author has of estimating the severity of the disease, varies from 94 to 97 per cent. of those treated by this method, while there is a mortality of from 91 to 100 per cent. in those untreated. J. H. M., Jr.

THE NUTRITION OF THE FETUS. By. J. MORRIS SLEMONS, M.D. Pp. 49. New Haven: Yale University Press, 1919.

IN a broad, general way, Dr. Slemons discusses in this monograph the results of the various chemical analyses of the blood of the

mother and fetus made by himself or his assistants during the past few years. We owe much of our present knowledge of the physiology of the placenta and of that fascinating problem, the metabolism of pregnancy, to the careful scientific investigations of the author. One will find here a most readable account of the mechanistic hypothesis of the placental function, the source and mode of transmission of the food of the fetus and the disposal of its waste products.

P. F. W.

THE HEART, PAST AND PRESENT. By EDGAR LEA, VICT., M. R. C. P. (Lond.), Honorary Physician and Physician-in-Charge, Cardiac Department, Ancoats Hospital, Manchester. Pp. 300. New York: William Wood & Co., 1919.

ACCORDING to the author this volume is in the nature of an inquiry. He has attempted to evaluate, from a study of the past, methods which promise most for future advances in clinical cardiology. He concludes that clinical methods of investigation have been and will be more fruitful than the methods of physiology and pathology.

An elaborate so-called clinico-etiological classification is offered, based not only upon symptoms or physical signs, but the type of cardiac failure in its relation to its exciting cause. Obviously, the attempt to employ such a classification reveals much of the deficiency in our present knowledge, toward which, Dr. Lea believes, intensive clinical inquiry should be directed. To facilitate these studies, he advocates special "heart clinics" in general hospitals, or if found feasible, institutions devoted to cardiac work.

The book reveals the author's enthusiasm for cardiology and his extensive knowledge of the subject. The discussion of heart failure is especially valuable. The point that factors other than mere muscle failure are often most important is stressed. The remarks concerning the relation of acidosis and anoxemia to cardiac disease would better have been omitted; certain of the hypotheses employed already have been rendered dubious.

C. C. W.

HALF A CENTURY OF SMALLPOX AND VACCINATION. By JOHN C. MCVAIL, M.D., LL.D. Pp. 87. Edinburgh: E. and S. Livingstone.

THE volume comprises the Milroy Lectures, delivered by Dr. McVail before the Royal College of Physicians of London on March 13, 18 and 20, 1919, and an Appendix containing a letter from Dr. C. Killick Millard upon this subject.

The book is divided into three main portions. The "natural

division" has been followed, each lecture being given a separate section. The three main headings are as follows: Smallpox as it was and is; vaccination as it was and is; control of smallpox in the present day.

The brochure deals particularly with the subject of smallpox and vaccination in England and Scotland, although references are made to the disease in other countries. Although the efficacy of vaccination does not have to be emphasized, the account of a school epidemic mentioned in the present volume will prove instructive. "An unvaccinated child attended school while suffering from smallpox. In her class were 27 children, of whom (*a*) 6 had been vaccinated and revaccinated; (*b*) 13 had been vaccinated only in infancy and (*c*) 8 were unvaccinated. All those under (*a*) and (*b*) escaped attack. All those under (*c*) were attacked." "In the same room were 42 other scholars, of whom (*a*) 8 had been vaccinated and revaccinated; (*b*) 20 had been vaccinated only in infancy and (*c*) 14 were unvaccinated. All under (*a*) escaped attack, 5 of those under (*b*) were attacked, each of them being over eleven years of age, and 12 of the 14 under (*c*) were attacked."

Emphasis is given that vaccination offers immunity only for a certain period and revaccination at certain fixed periods is necessary. Neither infantile nor revaccination has ever been compulsory on the population of the United Kingdom. Infant vaccination is being more and more neglected. There has been, during the last fifty years, a great diminution in the fatality, the infectivity and the prevalence of smallpox in Great Britain. This diminution has progressed at an increasing rate of speed, particularly during the latter part of the half-century.

One cannot help but being impressed, in reading this interesting exposition on the subject, with the excellence of our vacccination laws. F. C. K.

QUARTERLY MEDICAL CLINICS. By FRANK SMITHIES, M.D., of the Augustana Hospital, Chicago. April, 1919. Vol. I, No. 2. St. Louis: Medicine and Surgery Publishing Company, Inc.

THE favorable criticism which the first number of *Quarterly Medical Clinics* received at our hands must be repeated in favor of the second number of the first volume. It would be captious, indeed, to call attention to certain omissions, such as, for instance, failure to report the result of blood culture in Case XVI, since the excellence of Dr. Smithies's work is apparent in this volume as in the preceding one. In this as in the first number of the *Quarterly*, cases are presented, laboratory tests detailed, differential diagnoses considered and the presumably correct diagnosis offered, conclusions being arrived at only after careful consideration of all the data at hand. E. H. G.

DISEASES OF NUTRITION AND INFANT FEEDING. By JOHN LOVETT MORSE, A.M., M.D., Professor of Pediatrics, Harvard Medical School; Visiting Physician at the Children's Hospital; Consulting Physician at the Infants' Hospital and the Floating Hospital, Boston; and FRITZ B. TALBOT, A.M., M.D., Instructor in Pediatrics, Harvard Medical School; Chief of Children's Medical Department, Massachusetts General Hospital; Physician to Children, Charitable Eye and Ear Infirmary; Consulting Physician at the Lying-In Hospital and at the Floating Hospital, Boston. Second edition, revised. Pp. 384. New York: Macmillan Company, 1920.

NOTHING is more important to the student and practitioner of pediatrics than the acquisition of a practical knowledge of the processes underlying digestion and metabolism, so far as these have been accurately determined. It forms the logical introduction to the study of feeding and the clinical disturbances of digestion and nutrition.

In the second edition the authors have incorporated the results of recent research up to April 1, 1918; since that time, until publication, little of importance has been produced. Under the main headings: Physiology and metabolism, breast and artificial feeding, diseases of the gastro-intestinal canal and diseases of nutrition, the whole subject of infant-feeding and nutrition is succinctly and adequately considered. As a result of their extensive clinical and laboratory experience they have been able to adjudicate at times the discordant conclusions of different laboratory workers. Many important decisions as to the various factors in digestion and nutrition, of course, have to be reserved. Not the least valuable feature of the book are the indications afforded as to various lines of profitable research. J. C. G.

MENTAL DISEASES. A HAND-BOOK DEALING WITH DIAGNOSIS AND CLASSIFICATION. By WALTER VASE GULICH, M.D., Assistant Superintendent, Western State Hospital, Fort Steilacoom, Washington. First edition. Pp. 139; 36 illustrations. St. Louis: C. V. Mosby Company, 1918.

THIS book offers a classification of mental diseases which has been adopted by the American Medico-Psychological Association. Each subject is briefly considered, too brief, in fact, to be of any advantage to the average physician and not sufficiently accurate as to symptomatology, pathology or diagnosis to be of value to the psychiatrist. The facts pertinent to symptoms are not carefully arranged and the fundamental principles are lacking. The book is unscientific and too superficial to be practical. T. H. W.

SURGICAL CLINICS OF CHICAGO. December, 1919, Vol. III, No. VI. Pp. 215; 63 illustrations. Philadelphia and London: W. B. Saunders Company.

THIS number of the *Clinics*, by reason of containing the index for the volume, is a little reduced in reading matter. It is, however, well up to the standard. Several of the articles are extremely interesting, bearing on some of the most vital questions arising every day in operating. Some clever tricks of technic peculiar to individual operators are described.

This (December) number rounds out the volume for the year, and no surgeon will make a mistake in having the set upon his library shelves. E. L. E.

DISEASES OF THE STOMACH AND UPPER ALIMENTARY TRACT. By ANTHONY BASSLER, M.D., Professor of Gastro-enterology, New York Polyclinic Medical School and Hospital, etc. Fourth edition. Pp. 120; 881 illustrations and 73 plates. Philadelphia: F. A. Davis Company, 1919.

WE were disappointed in this fourth edition of what we believe to be almost the best of our English books on gastric disorders. The title page promised a revision and enlargement. As for revision, we could find none in the limited time at our disposal; as for enlargement we find the new edition containing no additional pages. About fourty-four new lines are devoted to a brief discussion on fractional test-meal examinations and about twenty-five new lines to reversal peristalsis. Both of these topics are timely and interestingly treated. Besides this, four new plates have been added to this edition, showing various normal and abnormal curves obtained by the fractional methods of gastric extraction.

The purchaser of this edition will believe that he has a completely revised work, when such revision has been very scanty. We have long since used this book, and use it much in every-day work. Perhaps it needed no revision or more additions—still, we feel for the doctor and his well-known gullibility. Why not say this work has stood the test of time and the former edition has been exhausted; we are reprinting it with a few additions to cover the recent advances which have been made in this field.

This edition, like its predecessors, treats very exhaustingly of all the common and uncommon conditions which one meets in gastric and upper alimentary diseases. The author has had a wide experience in this specialty, and adds a wealth of personal touch to the text. The illustrations are splendid; many of the roentgen-ray plates were made by Dr. Bassler himself. We will continue to recommend the book and refer to it in personal work.

T. G. S.

THE URETHROSCOPE IN THE DIAGNOSIS AND TREATMENT OF URETHRITIS. By N. P. L. LUMB, M.D., Major, R. A. M. C. (T. C.). First edition. Pp. 51; 42 illustrations, 39 in color. New York: William Wood & Co.

THE real value of this little treatise, and one in which it is not only unique but a decidedly welcome contribution to our knowledge, lies in the fact that its author has appreciated that you cannot teach the subject by didactic lectures nor by verbal descriptions, and while actual clinical experience is the best of all teachers in the subject, the next thing to such practical instruction is a presentation of the subject by copious illustrations, and in this feature Dr. Lumb's book, with its thirty-nine urethroscopic pictures in color, will ever be a valuable guide to the beginner, the teacher and the specialist.

He unfortunately describes in his brief test (in reality only thirty-eight printed pages) an instrument little known in America, the Wyndham-Powell air-dilating urethroscope, though the conditions he so ably illustrates are true to those seen through any of the instruments in daily use in this country. A. R.

A HAND-BOOK OF GYNECOLOGY. FOR STUDENT AND GENERAL PRACTITIONERS. By BETHEL SOLOMONS, B.A., M.D., F.R.C.P.I.; Gynecologist to Mercer's Hospital, Dublin. Pp. 236; 196 illustrations. New York: William Wood & Co.

THIS book represents a collection of the author's lecture notes which he has endeavored to place before the profession in tangible form. Of course, in a small volume it is manifestly impossible to deal extensively with the various subjects considered, but the author appears to have devoted too much space to academic and unessential classfications at the expense of diagnosis and treatment. The views expressed are in many instances too ancient to allow the book to be considered abreast of the times. Perhaps it is conservatism on the author's part in almost ignoring the value of radium in the treatment of gynecological diseases and in preferring to look askance upon Hitschmann and Adler's monumental work on the endometrium; but when he recommends curettage promiscuously and dilatation of the uterus by laminaria tents we must take exception to such teaching. The illustrations are simple line drawings, but fulfill their purpose. This book may be of great value to the author's own students when supplemented by considerable collateral reading and didactic teaching, but it can hardly be conceived that it would ever appeal to the American student who has been brought up to expect the best in medical books. F. B. B.

PSYCHIATRIC NEUROLOGICAL EXAMINATION METHODS. By DR. AUGUST WIMMER, Director St. Hans Hospital, Roskilde, Denmark. Authorized translation by DR. ANDREW W. HOISHOLT, Medical Superintendent, Napa State Hospital; Professor of Psychiatry, Medical Department, Leland Stanford Junior University, San Francisco, California. First edition. Pp. 172 St. Louis: C. V. Mosby Company.

THIS small book gives an excellent outline of neuropsychiatric examination. For example, when discussing ophthalmoscopic examinations it tells what examination should be made and gives a short explanation in what conditions choked disk, optic atrophy, etc., are found. It does not by any means essay to be a diagnosis.

The book has been well translated and the work is well done, but the reviewer questions whether such a book is of value. The general practitioner will not find it sufficiently explanatory. It cannot, of course, be intended for the neurologist, and the average student will have none of it. T. H. W.

PRINCIPLES OF HYGIENE, WITH REGARD TO THE GERMAN EMPIRE AND AUSTRIA. By DR. W. PRAUSNITZ, Eleventh, improved and enlarged edition, with 284 illustrations. Munich: J. F. Lehmann, 1920.

THIS is the eleventh edition of this book, containing 671 pages. It is printed on rather soft paper. The text is clear but the illustrations are not as distinct as could be desired, because of the cheap quality of paper used.

Following a brief introduction to hygiene, there is a chapter on the microörganisms. Then the following subjects are taken up in sequence: Air, weather and climate, clothing, baths, soil, water, housing, heating, ventilation, lighting, refuse matter, care of the dead, hospitals, child hygiene, school hygiene, nutrition, infectious diseases, industrial hygiene, race hygiene and social activity of the physician.

In general the book has undergone but slight revision from earlier editions, as indicated by the sub-title and the almost complete absence of advances in so many lines of the practical application of newer discoveries during and since the war. Although the fundamental principles presented in the book are sound, it is a source of regret that the enormous strides in our knowledge during the past five years remain unnoted, except in several minor particulars.

Since all the books by American authors dealing with the subject of hygiene have been kept up to date, and present, in more or less detail, the valuable experiences during the war, Prausnitz's book can have no interest for our readers because the contents of the book are largely out of date. D. B. H.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

ROGER S. MORRIS, M.D.,

FREDERICK FORCHHEIMER PROFESSOR OF MEDICINE IN THE UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO,

AND

THOMAS ORDWAY, M.D.,

DEAN OF UNION UNIVERSITY (MEDICAL DEPARTMENT), ALBANY, N. Y.

Typhoid Fever in the American Army in the Great War.—Russell (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1863) has presented some very interesting statistics concerning typhoid fever. The most instructive of these is a comparison of the actual deaths due to typhoid fever, malaria and dysentery in the Great War with the mortality which would have accrued had the death-rate been the same as in the Spanish-American and the Civil Wars. There were actually 213 deaths from typhoid fever in the American Army between September 1, 1917, and May 2, 1919. Had the Civil War typhoid death-rate obtained there would have been 51,133 and had the Spanish-American War typhoid death-rate obtained there would have been 68,164 deaths. He concludes: "It is evident from these tables, therefore, that antityphoid vaccination, carried out as it was . . . gave a high degree of protection to our forces . . . and reduced the (death) rate not only below the rate for previous wars but also below the rate found in civil life in some of the older States where the entire population is protected by all the sanitary measures of modern life."

Use of Air in Roentgenography.—Rautenberg (*Deutsch. Arch. f. klin. Med.*, 1919, cxxix, 296) describes the practical value of introducing air into the peritoneal cavity and then making roentgenograms. The procedure is simple and harmless and, in the four cases of liver disease reported, gave very valuable information. The size and shape, and in general, the consistency of the liver may readily be determined and con-

sequently, in some instances, a doubtful diagnosis may be confirmed. The method was first described by RAUTENBERG (*Deutsch. med. Wchnschr.*, 1914, xl, 1205), but remained unnoticed until 1918, when GOETZE (*München. med. Wchnschr.*, 1918, No. 35, quoted from S. and G.) described it as a new method of diagnosis. SCHMIDT and GOETZE (*Deutsch. med. Wchnschr.*, 1919, xlv, 201) have amplified the method and have carefully described the technic. DANDY (*Ann. Surg.*, 1918, lxviii, 5, and *Johns Hopkins Hosp. Bull.*, 1919, xxx, 29) describes a new method of unusual value in the study of brain tumors, etc. It consists of the introduction of air into the cerebral ventricles followed by roentgenography of the cranium. The procedure is called ventriculography. PFAHLER (*Am. Jour. Roentgenol.*, 1919, vi, N. S., 371) has shown that air may be used as a means of diagnosing certain bladder conditions. The technical details and many photographs will be found in the articles. The use of air as a partially opaque medium to roentgen rays while yet in the experimental stage has proved of considerable clinical value in the study of certain abdominal conditions, but perhaps of more value in the localization of brain tumors.

Cardinal Principles of Cardiological Practice.—LEWIS (*British Med. Jour.*, 1919, ii, 621) gives a brief statement of the chief diagnostic signs in cardiac diseases essentially chronic. Some of his statements are of interest and importance: (*a*) "Where there is definite enlargement (of the heart) or aortic disease or mitral stenosis or fibrillation of the auricles, then the safe course for doctor and patient is to attribute any undue distress on exercise to a cardiac lesion." (*b*) "In young subjects, if there is no such immediate evidence of heart disease as I have named in last paragraph, then a deficient exercise tolerance should rarely, if ever, be ascribed primarily to the heart. To this class belong almost all patients who are supposed to be suffering from 'heart strain' and a large number of patients incipiently infected with tuberculosis or chronically infected by pyogenic organisms." (*c*) "In elderly subjects, if there is no sign of structural disease but a poor tolerance of exercise, the heart cannot be declared free of disease; on the contrary, the heart should be regarded as the probable seat of mischief. It is, of course to this class that many cases of grave angina pectoris belong: but it also comprises many myocardial cases, in which the chief symptom is not pain but breathlessness or undue fatigue." The indications for bed treatment of cardiac cases are (1) distress when walking leisurely, (2) when active infection is known to be present, (3) when drastic treatment with a digitalis body is required.

Lethargic Encephalitis.—L'HERMITTE (*Ann. de méd.*, 1919, vi, 506), in an article entitled "L'Encéphalite Léthargique," has carefully reviewed the whole subject under the name ophthalmoplegic encephalitis with narcolepsy. The present epidemic seems to have started in Austria in the winter of 1916–17, where the first cases were reported by von Economo. About the end of January, 1918, cases were reported by French and English journals. The reports multiplied rapidly. The cardinal symptoms are ocular paralyses, somnolence and fever. The ocular palsies are often the first symptoms; the III pair is often unaffected, but if affected never totally. The paralysis may migrate from

one eye-muscle territory to another. Somnolence may precede or follow the ophthalmoparesis; it is seldom as deep as coma. It is pathological in that the patients attempt to resist it. Delirium may be present. At times other pairs of cranial nerves are affected, especially the VII and occasionally a transient hemiplegia may occur. Certain motor difficulties as hypertonia, incoördination, asynergia, and tremor may occur. The tendon reflexes depend largely on the area occupied by the nervous tissue changes. Signs of meningeal irritation only occur early in the disease. The cerebrospiral fluid is usually normal. Fever is very variable. Pathologically the changes are most marked in the mesencephalon and especially in the locus niger. The cells of the corpus striatum, optic thalamus and the nuclei of the III, IV, V, VI and VII nerves show slight but definite changes as a rule. The white matter shows no change. There may be widespread dilatation of small blood-vessels with hemorrhagic areas and perivascular infiltrations by cells of various types. The remainder of the article considers the relation between the disease "nona" and lethargic encephalitis and other known forms of encephalitis. The article is a complete *resumé* of the subject to date and is well worth the attention of those interested in the present epidemic.

Specific Aortitis, Prognosis of.—Reid (*Jour. Am. Med. Assn.*, lxxiii, 1832) states that the disease is present in 5.5 per cent. of 1919, autopsied cases at the Massachusetts General Hospital. In the 61 instances studied, the Wassermann reaction was positive or suspicious in 45 cases. Shortness of breath and chest pain were present in all of the cases, and on the average symptoms had been present about a year and a quarter before reporting to hospital. Adequate treatment was carried out in very few cases. Iodides and mercury alone did not seem to arrest the process, but more intensive antiluetic therapy seems to produce promising results.

Blood-pressure, Arteriosclerosis and Contracted Kidney.—Harpuder (*Deutsch. Arch. f. klin. Med.*, 1919, cxxix, 74) has carefully studied the relation of blood-pressure, arteriosclerosis and contracted kidney in 1165 cases. Of these cases all but 17 were past forty years old. He concludes from the study of clinical and pathological material that arteriosclerosis alone does not cause hypertension even if the smaller renal and cardiac vessels are involved. But that renal changes produced by the sclerosis of the smaller vessels lead to arterial hypertension. The appearance of hypertension is independent of the severity and extent of the anatomical lesion. Every patient with persistent hypertension has already a renal injury.

Progressive Hypertrophic Neuritis of the Adult (Non-familial).—Roussy and Cornil (*Ann. de méd.*, 1919, vi, 296) report acase, aged forty-four years, negative personal and family history. Began at forty. Marked atrophy of muscles of arms, with Aran-Duchenne hand and fibrillary twitchings. R. D. in nerves attacked. Ataxia, especially on left; more marked in arms. Romberg +. Intention tremor of arms. Sensibility slightly affected in left hand. Achilles and left patellar jerks absent. Periosteoradial reflexes absent. Pupils normal. Many

peripheral nerves greatly thickened. Section of nerve showed: (1) degeneration of myelin sheaths; (2) proliferation of cells of sheath of Schwann; (3) alteration of axis cylinders; (4) numerous small regenerating axis-cylinders; (5) hyperplasia of connective tissue. Wassermann reaction in C. S. F.+. The case differs from the Marie or the Déjerine type.

The Tarisch-Herxheimer Reaction.—HESSE (*Wien. klin. Wchnschr.*, 1919, xxxii, 439). The Herxheimer reaction is not characteristic in the sense that it is specific either for lues or for a certain drug, because it may occur during the treatment of non-specific dermatoses by mercury. This is proof that the reaction is not due to the flooding of the blood by endotoxins produced by the sudden death of large numbers of spirochetes. The reaction may be due to the injury of endothelial cells by the drug used.

Cerebral Disturbances Following Wounds of the Carotids.—ROHARDT (*Deutsche Ztschr. f. Nervenh.*, 1919, lxiv, 39) says that the fatality in carotid wounds usually results from hemorrhage or from anemia, and one seldom sees the cerebral complications. The mortality is about 50 per cent., but sinks to 10 per cent. under favorable conditions, that is, when early ligation can be done without infection. Death is due to anemia of one hemisphere. In many instances, after an interval, sometimes of several weeks, symptoms of a cerebral lesion appear. In general about two days elapse. The area of softening depends upon the adequacy of the collateral circulation. If the carotid is only partly occluded, the early functional disturbances may recede. Two of the cases reported had neck wounds and cerebral disturbances without obvious carotid wounds. In one of these there developed a carotid aneurysm, in the other a partial thrombosis. In both instances the cerebral symptoms were due to emboli. In the other two cases the carotid was ligated. In one there developed a left VII paresis, paresis and tactile agnosia of the left arm, apraxia of the left hand and a pseudobulbar speech defect. In the other case a period of six weeks elapsed before the appearance of a right optic atrophy and Horner complex.

The Pathology of Commotio Spinalis.—JAKOB (*Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1919, li, 247) states that the *commotio spinalis* and *contusio spinalis* merge one into the other. A soldier had a through-and-through abdominal wound at the level of the XII dorsal vertebra, with sensory and motor paralysis below L. seg. III. There were lesions of more than one spinal segment, *i. e.*, the sensory and motor disturbances were different at different levels. Sudden death from rupture of traumatic abdominal aortic aneurysm. Autopsy, a slight comminution of the XII dorsal lateral process. The cord showed diffuse nerve fiber degeneration in the white matter of the sacral and lower lumbar region; marked swelling of the tissue; many necrotic patches in the gray matter; ganglion cell changes and glia proliferation. A few small hemorrhages. The entrance zones of posterior roots showed changes. The author thinks this instance supports his and others experimental and clinical conclusions that the symptoms in *commotio* are due to actual traumatic lesions of cord rather than to hemorrhage.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

The Good Surgeon.—CRILE (*Ann. Surg.*, 1919, lxx, 385) says that the surgeons and pathologists who for years have intensively studied war wounds have formulated many theories of treatment—many apparently contradictory theories. He thinks that out of the present wide divergence of opinions the same fact that emerged from the post-Listerian period is emerging now—that the one agent of successful surgery is the good sound surgeon. Sound surgery means quick, innocuous, timely intervention; it means clearly the tomorrow of the wound; it means no intervention unless there is to be a net gain; it means a sharp knife, a good anesthetist, a painless, innocuous dressing.

Roentgenography of the Brain after the Injection of Air into the Spinal Canal.—DANDY (*Ann. Surg.*, 1919, lxx, 397) has previously shown that the cerebral ventricles can be outlined by a roentgenogram if injected with air. When doing this he noted that in many cases air could be seen in filaments on the surface of the brain. This must have followed the normal pathway by which the cerebrospinal fluid circulates. These observations gave promise of new possibilities in intracranial diagnostic study, because many lesions of the brain affect part of the subarachnoid space directly or indirectly. By substituting air for cerebrospinal fluid through a lumbar puncture all parts of the subarachnoid space can be clearly seen in a roentgenogram. Not infrequently an air shadow will completely surround the cerebellum, showing clearly its shape and size. The spinal cord can also be surrounded by a column of air. If the subarachnoid space is intact the air will always fill the cerebral sulci if given by an intraspinous injection. Frequently the exact position of the obstruction in the cisternæ can be seen in the radiogram. By its use one can detect whether or not a case of hydrocephalus is of the communicating type or not. This procedure is not devoid of danger if the amount of air is in excess of the fluid withdrawn, and this is especially true of intraspinous injections. The position is especially important, the head being at least 20 degrees higher than the needle.

Fracture of the Skull, with Special Reference to its Neurologic Manifestations.—WILENSKY (*Ann. Surg.*, 1919, lxx, 430) reports 75 cases of fracture of the skull admitted to Mt. Sinai Hospital, New York, where neurological cases, including skull fractures, have been segregated into a separate service. The great majority occurred in the first decade of life, and there were three times as many in the male as in

the female sex. The actual mechanism has almost always been a direct blow. The extent of the fracture varied greatly. Many were bursting fractures, probably, from direct impact through the lower jaw. Of the locations determined through the roentgen ray the most frequent sites were the parietal, frontal, frontoparietal and parieto-occipital regions. Most were simple fractures, but they frequently involved more than one of the bones. The fissures were usually vertical or oblique behind the coronal suture, those in front of the coronal suture running downward and forward toward the anterior cranial fossa. In one of the cases the edges were separated so far as to allow the dura to project between them. Comminution with depression was present in 8 cases. In the cases coming to operation the subjacent brain was often found to be injured with or without laceration of the overlying dura. The brain damage often exceeded that of the skull. One case demonstrated the contre-coup mechanism. Roentgenographic studies were made of all cases, except those admitted in a moribund condition. The symptoms of brain irritation were not always present. The variation of symptoms was wide, vomiting and headache being the most frequent. In all cases except those with scalp wounds which disclosed fractures only by the roentgen ray, there was a transient or persistent loss of consciousness. This depended upon the degree of concussion or compression. A number of cases developed fever without any apparent source of infection, the highest temperature being 109° F. This was probably due to brain trauma. The general neurological symptoms were varied. Twelve patients died of concussion within a few hours of the accident. Compression phenomena were common and usually appeared quickly. In judging the severity of the increase in intracranial pressure, the greatest reliance was always placed on the condition of the circulation, and a marked increase of pressure was the most imperative indication for operation. Generalized convulsions were present in only 1 case. The reflexes were frequently altered, but often had no bearing on the total clinical picture. Thirteen cases showed abnormalities of the external or internal ocular apparatus. Three cases had unilateral exophthalmos. Eleven had abnormalities of the fundi. The cranial nerves were involved in 7 cases, the orbital in 2 and the facial in 5 cases. Focal symptoms of the extremities were present in 4 cases. The longitudinal sinus syndrome, a spastic paraplegia, was present in 6 cases. In all these cases the injury was near the vertex. Various complications, such as intracranial hemorrhage, leakage of cerebrospinal fluid and meningitis were met. It was not considered imperative to operate on all compound fractures, except to debride the wounds. According to the symptoms exhibited, unilateral or bilateral exploratory craniotomy or a craniotomy plus a contralateral subtemporal decompression was performed. Lumbar puncture was not done routinely, as it did not seem to give any added information. Of the 72 cases, 22 died (31 per cent.). Eighteen were operated on, with a mortality of 48 per cent. Of those treated conservatively the mortality was 27 per cent. Wilensky does not think that operation, skilfully done, adds anything to the risk. Conservative and expectant treatment, whenever they can be safely employed, yield the best results. Operation is imperative in every case showing signs of increasing intracranial pressure, as irritative or paralytic focal symptoms.

Treatment of Chronic Empyema.—WATTENBERG (*Ann. Surg.*, 1919, lxx, 552) reports the results of treatment in 121 cases of chronic empyema at General Hospital No. 26, Fort Des Moines, Iowa. Practically all the cases in this series had had an operation, most commonly rib resection, before admission. The following factors were of vital importance: Adequate drainage was accomplished in some cases by dilation of an already existing sinus by the introduction each day or two of a slightly larger drainage tube than that previously in place. This dilation was continued until the tract was of sufficient size to admit six to eight Dakin's tubes and at least one overflow drainage tube one-quarter inch in diameter. In cases in which the density of the scar tissue above the sinus or the reformation of the resected rib had closed the opening to such an extent that an ample opening could not be obtained, an operation was performed. An incision was made along the course of the rib above the sinus and the rib was resected for a distance of two to two and one-half inches. Any bone interfering with drainage was removed. The pleura was found to be thickened by a tough, fibrous exudate. It must be excised to obtain competent drainage. Simple incision through a thickened pleura is followed by too rapid healing to ensure a good result. In certain cases this organized exudate practically filled the cavity. It was dissected out with the fingers and removed. Dakin's tubes and overflow tubes were then inserted and held in place by gauze tightly packed into the external orifice of the wound. The next factor after drainage was the careful sterilization of the cavity by the installation of Dakin's fluid. The whole cavity was flushed out once a day by the chlorin preparation. The cavity was filled to overflowing with this solution every hour by day and second hour by night. The patient was instructed to shift his position freely during each instillation. The skin was carefully protected against burning by the solution. The sterilization of the cavity was determined by bacterial controls taken twice a week. When a cavity was found to be sterile on seven successive days, the tubes were removed, gauze tightly packed into the external orifice and the cavity permitted to close. The streptococcus hemolyticus was found in 100 per cent. of cases. The cavities never closed spontaneously while this organism was present, but often did so (62 cases) after this organism had disappeared, though other bacteria were still present. Wattenburg thinks that a bronchial fistula is no contra-indication to the use of Dakin's solution. By careful handling the fistulæ healed under this treatment. The third essential factor in the treatment of chronic empyema is high caloric feeding. Blowing exercises with Wolfe's bottle and graduated calisthenics aided in the expansion of the chest on the affected side. In all 201 cases were treated. All but 27 healed under the treatment outlined. Three of these closed permanently two months after the tubes were withdrawn. Two were definitely tuberculous and three are still under treatment without drainage. Seven are receiving further Dakin treatment. Three died. Twelve were transferred to other hospitals before this treatment was completed.

Infections of the Knee-joint.—ORR (*Surg., Gynec. and Obst.*, 1919, xxix, 492) found that knee conditions in France presented themselves in two principal forms: (1) The so-called internal derangements, and

(2) the acute infections. He deals with the second group, which he divides into four varieties: (1) Acute infections of the joint, with the formation of pus but no opening into the joint; (2) compound injuries to the joint but no damage to the bone; (3) compound fracture of the femur or tibia involving the joint; (4) cases included in 2 or 3, with general sepsis supervening. In cases of the first variety, active and passive motion to an extent not causing pain, can be used after adequate drainage has been instituted. In only a few cases of the second variety and in no cases of the third and fourth varieties should an attempt be made to secure a movable knee-joint. Ankylosis is the end to be sought, with the knee at an angle of from 10 to 20 degrees. Attempts to secure motion except by late arthroplasty should be discouraged, except in group one.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.

NEW YORK,

AND

CHARLES C. LIEB, M.D.,

ASSISTANT PROFESSOR OF PHARMACOLOGY, COLUMBIA UNIVERSITY.

Local Serotherapy of Gonococcus Rheumatism.—DEHRÉ and PARAF (*Bull. de la Soc. méd. des. Hôp.*, 1919, xliii, 908) describe in detail 15 cases of acute gonococcus arthritis treated by injections of antigonococcus serum into the affected joints. In 6 cases the cure was complete in less than eight days; in 8 others before the fifteenth day. The joint function returned to normal in a rapid and apparently complete manner. This treatment is limited to the larger joints because of the difficulty of injecting the serum into a small joint. They puncture the joint and inject the serum in place of the effusion. This was repeated every day or every second or third day. In the case of multiple joint affections they were all treated at the same time in the same way.

Harmful Effects of Shallow Breathing, With Special Reference to Pneumonia.—From observations on a number of cases of pneumonia, MEAKINS (*Arch. Int. Med.*, 1920, xxv, 1) concludes that the anoxemia occurring in acute lobar penumonia is the result of the rapid and shallow breathing typical of this condition. It is well known that the severity of the symptoms in pneumonia is not necessarily dependent on the degree of pulmonary involvement. A much more valuable indication as to prognosis is the respiratory-rate. It has been observed that as the respiratory-rate increases the patient's condition becomes more grave. As a rule, in adults when the respiratory-rate persists above 50 per minute, cyanosis begins to develop. This is a definite sign of pronounced anoxemia. The harmful effect of persistent anoxemia on

the cardiovascular system is well recognized. There is no particular proof that the cyanosis in pneumonia is due to cardiovascular failure, and careful observation leads the author to believe that the cardiovascular collapse is a sequel to the anoxemia. In spite of the gradual increase in the total volume of expired air per minute there is a very conspicuous diminution in the ratio between the respiratory volume and the theoretical dead space until a point may be reached where the alveolar air, expired or inspired, amounts to comparatively few cubic centimeters, being undoubtedly insufficient to carry on any adequate pulmonary ventilation, so that eventually cyanosis develops. The respiratory quotient becomes progressively higher, but when the crisis occurs there is a rapid return to normal not only in regard to the respiratory quotient but also in the respiratory-rate and volume and the total ventilation per minute. Another aspect of the question is the part played by the pulmonary circulation. While it must be assumed that a certain volume of blood passes through the damaged lung area without proper ventilation, we are not justified in supposing that this non-ventilated blood is sufficient in amount to reduce appreciably the oxygen content of the mixed blood entering the left side of the heart. Therefore the author concludes that the anoxemia occurring in pneumonia is the result of the rapid and shallow breathing.

Acute Methyl Alcohol Poisoning Associated with Acidosis.—Harrop and Benedict (*Jour. Am. Med. Assn.*, 1920, lxxiv, 26) report a case of severe acute poisoning with methyl alcohol associated with a marked grade of acidosis, in which recovery followed the use of alkali therapy. The acidosis was associated with an increase in the amount of titrable organic acids in the urine and specifically with a marked increase in the excretion of lactic and of formic acids. The authors cite an observation of Bongers, who gave methyl alcohol to dogs by mouth and was able to recover about three times as much methyl alcohol in the combined washings of the second and third days as he was able to obtain in those of the first. This work would appear to clearly indicate the importance of thorough and repeated lavage.

The Basal Metabolism in Exophthalmic Goitre.—This paper by Means and Aub (*Arch. Int. Med.*, 1919, xxiv, 645) is based on 345 metabolism observations on 130 patients. These observations bear out the conclusions drawn in their first paper on the subject. In addition, using the basal metabolism as an index of toxicity, they find that: (1) In the majority of cases the results after two or three years are equally good with roentgen-ray treatment as with surgery. (2) After surgery the metabolism shows a rapid preliminary fall, a secondary rise followed by a final fall; with roentgen-ray treatment there is a gradual progressive fall. (3) In securing the same end-result with surgery or with the roentgen ray, a lesser rest factor is necessary with the latter. With the roentgen ray there is practically no mortality; with surgery there is a definite one. (4) Patients treated surgically do better and the risk of operation is less, if they have previously had their thyroid and thymus glands irradiated. (5) The risk of operation

is greater and the need for preoperative roentgen-ray treatment is greater in cases with a very high metabolism and moderate tachycardia than in those with an extreme tachycardia and moderate metabolism elevation. (6) The safest progam for the treatment of exophthalmic goitre, as a whole, is the routine irradiation of thyroid and thymus glands, in all cases, with surgery held in reserve for patients who do not then do well. (7) Surgery is contra-indicated with patients whose metabolism is rising in spite of complete rest in bed, and also with patients of the type with moderate tachycardia and great metabolism increase, except when they have previously had thyroid and thymus glands treated by the roentgen ray. (8) Finally, they believe that in the management of exophthalmic goitre, periodic determination of the basal metabolism should be quite as much a routine as is the examination of the urine for sugar in diabetes mellitus. Further, in border-line cases they believe the basal metabolism furnishes very valuable aid in differential diagnosis.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,

OF PHILADELPHIA.

Thymus Study.—PARKE and MCCLURE (*Am. Jour. Dis. Children*, November, 1919) have made an exhaustive review of the literature on the thymus gland and also publish the results of their own experiments, comparing the work of their predecessors with their own. Their work was undertaken in the belief that it was possible to produce in animals a rickets almost, if not quite, identical with human rickets by means of the removal of the thymus gland. As regards the former literature it is doubtful whether an unprejudiced person who read for the first time the articles on extirpation of the thymus, could obtain from it any clear conception as to what the effects of removal of the thymus actually are. He would probably be at a loss to know whether to regard the thymus as essential to life or as an organ devoid of function, or at least of function demonstrable by extirpation. Unfortunately the more recent experimental work on thymus function has not brought the problem any nearer solution. Indeed it has been productive of more widely divergent results than the earlier work. Some of the causes of the confused state of our knowledge concerning the effects of the removal of the thymus may be laid to the fact that a large amount of the experimental work connected with extirpation of the thymus has been inadequate. The experiments of the earlier and more recent investigators who have depended for the removal of the thymus on the method originally employed by Friedleben, cannot be accepted as valid for the determination of the function of the thymus, for if extirpation performed by that method is even approximately complete, it cannot possibly be so with any regularity. The experiments of others who employed better operative methods are of little value or actually worthless because of

the careless manner in which they were conducted, the use of unsuitable experimental subjects, the lack of sufficient control animals. It is also apparent that a number of investigators have drawn conclusions in regard to the effects of removal of the thymus from experimental data which are wholly inadequate, and have not only increased the number of erroneous conceptions, but have planted them firmly in literature. Soli, for example, inferring that the thymus exerts a regulating influence over the growth of bone in very young but not in older animals, as the result of one experiment on a rabbit two months old, or Seimhuber stating that the thymus is non-essential to life from experiments on two dogs, neither of which appeared to have been necropsied in order to make certain that the extirpation had been complete, are only two of a number of possible illustrations. Experiments so limited that chance variation of dietetics or environmental influences cannot be excluded as the controlling factors do not prevent of any induction concerning thymus gland function. Few seem to have hesitated to draw hard and fast conclusions of inadequate facts. It is also manifest that a number of investigators have placed overvaluation on positive experimental results at the expense of negative experimental results. Those who have done this seem to have started out with the assumption that the thymus possessed a function susceptible of demonstration by means of extirpation, and that negative results are, from the very nature of things, meaningless. Accordingly in forming conclusions they have considered only positive results. It must be clear to everyone that in this particular field of investigation the positive experimental results which have been obtained do not have more significance than the negative results, inasmuch as they have not consisted in the development of changes in thymectomized animals which are not specific but may be brought about in other ways than by the removal of the thymus gland, or may develop spontaneously. In this way it has come to pass that a discrepancy has arisen between the actual results of the experiments themselves and the conclusions drawn from them, which appears not on the surface but becomes apparent after study of the experimental literature. If only conclusions which investigators have drawn from their experiments are considered, as is the case in almost all discussions or presentations of the thymus problem in the literature, a false impression as to the actual experimental results is obtained. The causes reviewed above in explanation of the confusion of ideas which exists concerning the effects of thymus extirpation cannot be regarded as having been more than contributing factors. Undoubtedly the fundamental cause lies in the difficulties inherent in the problem itself. The diverse character of the results from the same procedure is sufficient proof that either the elicitation of evidence of thymus function is exceedingly difficult, or else that the thymus is possessed of no function or of no function that is demonstrable by extirpation. The only certain knowledge in regards to the removal of the thymus up to the present time afforded is surprisingly small and may be stated as follows: The thymus is not essential to life in the frog and its complete removal from that animal causes no alteration in bodily growth or development; similarly the function of the thymus gland is not necessary to life in the rat and its destruction in that animal produces no demonstrable alteration in growth or development or any changes of a morphological nature

in any of the organs, as judged by the ordinary methods of histologic study. Few of the positive results of thymectomy have actually been proved to be false. It is certain only that the remarkable train of symptoms ending in death which Abelous and Billiard, and later Camia, announced they obtained in the frog, and those of Magini, Klose, Flesch in the rat, must have been due to other causes than deprivation of thymus function. The reported results of thymectomy fall roughly into three groups: In one, removal of the thymus has been found to be without effect; in another removal has been followed by transitory disturbances in health and development; in the third removal has brought about death with or without changes in growth and nutrition, and alterations in the skeleton, and in certain of the organs, particularly those of internal secretion. A considerable number of observers have been unable to detect any change, or at least, any change of significance following thymectomy. Comparatively few have discovered that removal of the thymus produced death, and not a single one has found that thymectomy caused death invariably, or even in the majority of cases. Almost all of those who have reported positive results following extirpation of the thymus, have obtained negative results as well, the two kinds being intermingled in varying proportions. Though the changes reported by some have been limited to single pathological manifestations or to alterations in a single organ and have seemed to indicate that thymus activity was distinctly circumscribed, the changes reported by other investigators, particularly some of the more recent, have been in the nature of complex diseased states in which the whole animal was affected, and have seemed to imply that the function of the thymus was intimately concerned with the most fundamental of the bodily functions. The positive results obtained by some investigators seem to have little connection with the positive results obtained by the others, and in a few instances have been contradictory. Those obtained by some have a certain amount of similarity in that they center about changes in the growth and development of the skeleton such as overgrowth of the animal as a whole an increased growth of the skeleton; retardation in growth of the skeleton; retardation in growth with thickening of the bones of the skeleton; thickening of the bones with bowing; spontaneous fracture; reduced calcium content of the bones; pseudorachitic deformities; osteoporosis; osteomalacia; rickets. At least nine investigators have described in one or more thymectomized animals retardation in growth with rachitic-like deformities, especially in the long bones of the legs. Only two of them have given proof that the pathologic condition in the bones of their experimental animals was really rickets. One has shown on fairly good evidence that both the thymectomized and control animals of his experiments were affected alike with rickets. Several observers have reported alterations in the hair of their thymectomized animals, and several have described a voracity of appetite exhibited by the thymectomized animals in contrast to their control mates. A very few investigators have examined their material for alterations in the endocrine glands. Five have reported changes in the nature of hyperplasia in the thyroid and two have reported hypertrophy of the medulla of the suprarenal, but no one has reported pathologic developments which are of a convincing character in any of the other organs of internal secretion. Few seem to have studied the organs

of internal secretion with any care and no one has applied to the study some of the more recently developed histologic methods or made examinations in the period which immediately followed thymectomy. As a result of their own studies the authors show that the thymus gland is not essential to life in the dog. Extirpation of the thymus produces no detectable alteration in the hair, teeth, contour of the body, muscular development, strength, activity or intelligence of the experimental animals. Extirpation of the thymus probably does not influence growth or development. The possibility that it may cause retardation in development and delayed closure of the epiphysis cannot be excluded absolutely. Removal of thymus probably produces no alteration in the organs of internal secretion. It is possible that it produces well marked changes in the organs of internal secretion in the period immediately following thymectomy, an observation that was not covered by these investigators in their series of experiments.

Human Rabies.—REGAN and SILKINAN (*Arch. Diag.*, April, 1919) discuss this important topic from the standpoint of their recent experience. They found that the best method of treating the bites of suspected rabid animals is by cauterization. Many writers advocate the various caustics indiscriminately considering all of equal value. This is important as many of the more commonly used methods, such as cauterization with carbolic acid, silver nitrage and the thermocautery are objectionable in that they seal up the virus by coagulating the albumin of the tissue cells. Nitric acid does not possess this very serious disadvantage for by virtue of its power of diffusibility and penetration, it may destroy the virus in cases in which the other methods would have no results. It is especially valuable in the cauterization of bites treated late. It produces little scarring and the resultant wound heals well. It is the caustic that should always be employed. To get the utmost effects the nitric acid must be fuming. The wound should be cauterized as soon after the bite as possible. While many writers claim that to be effective cauterization must be employed within the first few hours after the bite, there is no experimental proof to show that certain caustics, notably nitric acid are effective at a much later period. Hence in cases in which the bite is seen late, nitric acid should be applied even up to the seventy-second hour after the accident. This is logical because it is well recognized that the virus progresses very slowly from the original atrium of infection. If only part of the effective material introduced is destroyed, the amount may be sufficient to allow the body to overcome the small portion of the virus unaffected by the cauterization. Prior to cauterization the wound should be squeezed to encourage bleeding and should be thoroughly washed with mercuric chloride solution 1 to 1000. A wet dressing of the same should be applied after the caustic has been used. If the wound is a punctured one and cannot be properly cauterized, it should be laid open with a scalpel to allow treatment. A bite should not be sewed up. If sutures have been introduced before the patient appears for treatment, they should be removed and cauterization performed. For ordinary bites nothing stronger than a three-day cord should be used. For face bites and extensively deep wounds a two-day cord should be employed. If the patient has been bitten by a positively rabid animal it is a practice to

advise a return for a second series of injections after six months. This will prevent those rare instances of death when the particular virus concerned has a long incubation period. In the case of face bites or very extensive wounds one of the writers of this paper has recently recommended that the entire course of treatment be repeated two weeks after the completion of the first.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,

AND

FRANK B. BLOCK, M.D.,

ASSISTANT INSTRUCTOR IN GYNECOLOGY, MEDICAL SCHOOL, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Trigonitis in the Female.—There is a large and common group of cases, in which the symptoms are chiefly those of bladder irritability with a clear urine and no gross intrinsic or extrinsic pathology to explain them. In these cases careful examination with the cystoscope will reveal definite changes in the trigone as the chief pathological feature and to this group of cases we apply the term cystitis colli or trigonitis. The onset is generally insidious with gradually increasing frequency of urination, especially by day, but somewhat also at night. With this there is usually no pain, but at the end of the act of urination there is generally a sensation of incompleteness and a desire to pass more. The patient will empty her bladder and within two or three minutes have an uncontrollable desire to urinate again which usually, if yielded to, accomplishes nothing or at most only a few drops are expelled. There is an almost constant desire to urinate and many patients complain that by day they are obliged to relieve themselves as often as every five minutes, voiding only a few drops each time. In the later stages there may be some pain but it is rarely very severe, and occasionally there may be a slight terminal hematuria. The treatment of these cases has always been more or less unsatisfactory, although many varieties of treatment have been advocated. The latest treatment of this condition, as described by LINDEMAN (*Surg., Gyn., and Obst.*, 1920, xxx, 64), consists of the injection of quinin and urea hydrochloride into the bladder mucosa. This treatment is based on the well known fact that this drug, when injected into the tissues, especially in a strength of over 1 per cent., causes a deposit of fibrin and a considerable induration at the point of injection which not infrequently remains for months. Furthermore the outstanding feature of the cystoscopic picture of this disease is intense congestion, hypertrophy and hyperplasia of the subepithelial bloodvessels and the swollen mucosa. Therefore Lindeman deduced that if anything could cause the destruction

or at least constriction or compression and thereby reduction in size and possibly in number of these bloodvessels, the disease would be relieved and he felt that the injection of quinin and urea hydrochloride could accomplish these objects. He uses a sterile 2 or 3 per cent. solution of the drug in normal saline solution colored with methylene blue (for technical purposes) and makes the injections by means of a very long flexible needle which is introduced into the bladder through the catheterizing channel of a cystoscope. The needle is inserted into the mucosa of the trigone, preferably near one of the ureters, and a few drops of the solution are injected, producing a small blue wheal. The needle is then inserted into other areas of the trigone and the process repeated until as much of the trigone as possible has been injected. He states that practically all of the patients that have had this treatment have been greatly relieved and many of them required no further treatment. There is one possible danger of this treatment and that is the tendency of this drug to cause necrosis of the tissues when injected under pressure, but thus far Lindeman has had no such untoward result although he realizes the possibility of this outcome.

Ruptured Ovarian Cyst Without Symptoms.—Rupture of ovarian cysts is not, of course, extremely rare but from the clinical standpoint the case reported by BEVAN (*Surg. Clinics of Chicago*, October, 1919, p. 1083) is of interest because there was a complete disappearance of a very large tumor without any symptoms. The patient was a woman, aged thirty-five years, who had been married a number of years but had never had any children. On examination she presented a large cystic tumor of the abdomen which was diagnosed as an ovarian cyst and operation was strongly urged. About two weeks later she returned and stated that the tumor had disappeared, that her clothes were four inches larger than they were before and that she had lost eight or ten pounds in weight. Examination at this time confirmed her statement as the tumor had completely disappeared and there was not even any mass palpable on bimanual examination. Bevan suspected a ruptured cyst and sent her to the hospital for operation and when the abdomen was opened a cyst of the left ovary was found which contained between two and three quarts of yellowish fluid and at one point the cyst wall was very thin and adherent to the cul-de-sac and Bevan believes that it was at this point that the cyst had ruptured. The total absence of symptoms, either at the time of rupture or subsequently makes this case an interesting rarity.

Ovarian Residue in Therapeutics.—For some time GRAVES (*Surg., Gynec., and Obst.*, 1919, xxix, 537) has been advocating the use of ovarian residue in the treatment of those conditions which are usually attributed to deficient ovarian secretion. By the term ovarian residue he refers to that part of the ovary which remains after ablation of the corpus luteum and which has usually been discarded as valueless. The results that he has attained with ovarian residue so closely parallel the effects obtained from whole ovary that it has been impossible to draw any definite conclusions in favor of one or the other preparation. He feels safe in stating, however, that the ovarian secretion is not solely confined to the corpus luteum since the secretion of the atretic follicles

and the corpus luteum is a similar product being manufactured by analogous cells, namely by those proliferated from the internal theca. Ovarian residue preserves its integrity longer than do those ovarian preparations which contain corpus luteum substance so that under present conditions of preparation ovarian residue is in general superior in its clinical results to the commercial articles now on the market. The case reports which are included in his articles are divided into three groups: (1) those exhibiting the symptoms of the artificial or natural menopause; (2) those treated for such menstrual disturbances as amenorrhea, oligomenorrhea, delayed menses and clotting; (3) those of essential dysmenorrhea. The majority of the cases of the first group were treated for postoperative hot flushes. In only a few of the cases were the symptoms severe, and in many they were not a source of complaint, being elicited only after questioning the patient. Ovarian residue was administered therefore, in many instances chiefly for the purpose of testing its effects on these characteristic vasomotor manifestations. For hot flushes, ovarian residue like the other ovarian preparations, acts as a specific palliative rarely failing to give some relief. For those multiple neurosecretory disturbances such as dizziness, sleeplessness, headaches, muscular pains, buzzing in the ears, asthenia, etc., which are so common in the natural, though not in the artificial menopause, ovarian residue is helpful in many cases. In this group there were 41 cases and the treatment exerted a beneficial action in 32 or 78 per cent. In the second group there were failures, especially in the long standing cases of amenorrhea, although in some instances of delayed menses and clotting the results were rather striking. Even in the amenorrhea cases in which the menstrual rhythm could not be reëstablished, the patients often mentioned the tonic effect of the treatment. The third group of essential dysmenorrhea is quite incomplete since he has only recently used the residue in the treatment of this important disorder. Although he is now treating a number of dysmenorrhea cases of the anteflexion type with the hope of avoiding operative interference, sufficient time has not elapsed to warrant definite conclusions.

Indications for Sterilization.—In considering the question of when sterilization in women is justifiable, PETERSON (*Jour. Mich. State Med. Soc.*, 1919, xviii, 608) calls our attention to the fact that there are two kinds of artificial sterilization of women—primary artificial sterilization and incidental artificial sterilization. In primary artificial sterilization, the end in view is solely to prevent future conception. Incidental artificial sterilization means the sterilization of the woman during the course of another operation in the belief that the patient's life or well-being would be seriously impaired by future pregnancies. Primary artificial sterilization should be comparatively infrequent, since the organic disease which calls for the operation at the same time renders it hazardous and in the uncertainty of the woman with organic disease requiring sterilization, the physician will hesitate to advise this procedure when the uterus can be emptied with less danger in case pregnancy supervenes. In incidental sterilization, the woman can be rendered sterile by a simple additional operative technic the dangers of which are practically *nil*. Peterson believes that all operations devised for temporary artificial sterilization are based upon wrong premises, since

the indications calling for sterilization are bound to grow worse, never better. As a rule a woman should never be sterilized without her consent and that of her husband, and of her family or other physician. Finally, careful study of the history of the patient, especially her puerperal history, her past and present condition, will enable the physician to decide for or against primary and incidental artificial sterilization in pulmonary or other forms of tuberculosis, diseases of the kidneys or heart, mental diseases, pelvic contraction, defects in the reproductive organs due to previous labors or operations, and operations of such nature that subsequent pregnancy and labor are rendered dangerous.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
OSKAR KLOTZ, M.D., C.M.,
PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

The Size of the Spleen in Immune Mice.—Although the literature is full of articles upon the part played by the spleen in the growth and development of tumors, it will be found that there is no evidence so far advanced for the significance of the spleen in resistance that cannot be matched with equally good evidence against its participation. WOGLOM (*Jour. Cancer Res.*, 1919, iv, 281) gives a brief review of the chief arguments as a preface to his work on this much debated subject. Underlying all the reports of an hypertrophied spleen in tumor-bearing or immune mice is the tacit assumption that the organ was of normal size before inoculation. However, a careful study of mice and the most common mouse infection (mouse-typhoid) will reveal the fact that very few strains are free from this disease and consequently mice which are generally considered normal have enlarged spleens. The author performed a series of experiments on mice to determine the average weight of a normal spleen. The direct measurements of the organ were made by laparotomy and in order to determine whether or not the spleen enlarged after the operation two sets of animals were autopsied two and seven weeks after the incision and first measurements were made. It was found that of the two-week animals 20 per cent. developed an hypertrophied spleen and of the seven-week 50 per cent. showed a still greater enlargement of this organ. The author makes allowances for both cage infection and infection at operation but is unable to come to any definite conclusions from the data at hand. He thinks it fair to assume that laparotomy does not result in enlargement of the spleen, when done with reasonable cleanliness. After extensive experiments in which mice were inoculated with various immunizing and non-immunizing materials the author is unable to adduce any positive results. The presence or absence of an enlarged spleen in natural, as in acquired immunity, is a matter of pure chance so far as susceptibility or resistance to tumors is concerned. Splenic enlargement therefore is certainly

the effect of extraneous factors and can often be traced to mouse-typhoid. The author is not able to bring forward any argument to refute that of those who believe that the lymphocyte plays an important role in establishing a tumor immunity. He thinks the spleen might be actively engaged and yet not show participation in so far as its size is concerned. All his experiments reveal only the fact that some immune mice have enlarged spleens and some have not; some animals with progressively growing tumors have enlarged spleens and some have not. And the existence of other causes of splenic hypertrophy, such as mouse-typhoid, transfers the burden of proof to those who assert that splenic hypertrophy is referable to immunity.

Dissemination and Destruction of Typhoid Bacilli Injected Intravenously in Normal and Immune Rabbits.—STONE (*Jour. Infect. Dis.*, 1919, xxv, 284) presents the results of investigation of the mechanism of destruction of typhoid bacilli in rabbits. The author reviews the different phases in the development of the knowledge of the typhoid bacillus in its various relations to the animal organism. Rabbits were injected through the ear vein, with measured quantities of living typhoid bacilli. It was found that injection of typhoid bacilli into normal animals was followed in a small percentage of cases by fatality. The typhoid bacilli were demonstrated in all organs within one-half hour, and persisted for about fourteen days, with the exception of the gall-bladder, where they persisted beyond the eighty-sixth day. Immune animals' blood and tissues were found to be sterile within twenty-four hours after a similar injection. Repeating the work of Bull and others, similar paradoxical results were obtained, showing the bactericidal property of normal serum and the lack of same in the serum of immune animals *in vitro*, regardless of the agglutinating titre. Addition of leukocytic suspensions to immune serum *in vitro* in the presence of B. typhi, produced no inhibition of bacterial growth. Reactivation of immune serum by the addition of fresh normal serum in the presence of B. typhi, showed increased inhibition of growth relative solely to the amount of fresh serum added. Admixture of macerated tissue from immune animals to broth suspensions of typhoid bacilli, produced no inhibition of growth. Details of technic are given.

On the Mechanism of Bacterial Infections, with Special Reference to Gas Gangrene.—BULLOCK and CRAMER (*Report of Imperial Cancer Research*, 1919, vi, 23) have carried out an extensive research for determining the critical factors associated with gas gangrene. Gas gangrene, they state, is a "severe local lesion accompanied by a toxemia and followed frequently by a septicemia." The organisms chiefly responsible are Bacillus welchii, Bacillus edematiens and Vibrio septicus. The experiments which were carried out in mice showed that the mere presence of these organisms in a wound is not sufficient to cause the peculiar tissue reactions. Thus when the Bacillus welchii obtained from cultures, is washed free from the medium and by-products and is then injected into animals, no reaction of the nature of gas gangrene is obtained. But when the organisms are inoculated along with the medium in which they have grown, the typical gangrene results. The culture medium contains the toxin which assists invasion. The authors

lay stress upon the "specific" effect of the toxin upon the adrenals, which they believe is most important in relation to the fatal outcome. Various factors (cold, exhaustion, fatigue, hemorrhage and anesthesia) place an extra strain upon the adrenals and may further assist in enhancing the influence of the toxin. The toxin of gas gangrene has two separate functions. At first it acts locally in the manner of an aggresin and enables the bacteria to establish themselves in the body; later it produces a specific toxemia which with other factors contributes to the lethal issue. In the ordinary mode of infection by these organisms toxin is not immediately available to permit invasive localization. Small numbers of these bacteria alone will not cause gas gangrene. The authors have found that the accessory factor in establishing the progressive infection lies in the presence of calcium salts which are so commonly introduced in war wounds with the infection. Other substances were also found to act in a similar but less active manner. Contact between the bacteria and the calcium salt is not essential. Gas gangrene will develop if the bacterial suspension and the calcium salt are injected at different times into the same site or into different sites at the same time or at different times. The calcium salts produce a local change in the tissues disturbing the defensive mechanism against these bacteria. Injury of muscle tissue is not essential for the development of gas gangrene. The authors explain the manner of the action of calcium salts as follows: "One factor which determines the course of an infection is related to the mechanism by which the leukocytes are first guided to the focus of infection so as to surround it and then having dealt with it, are removed again and enabled to dispose of the injected bacteria. This mechanism is evidently upset by the injection of calcium salts and substances having a similar rupturing (of local defense) action. From the lesions in the bloodvessels and lymphatics indicating a stasis and the production of a clot of lymph and plasma it seems reasonable to conclude, that the disturbance of the vascular and lymphatic drainage of the tissues is responsible for the disturbance of the mechanism which presides over the movements of the leukocytes toward the focus of infection and away from it."

Observations on the Functional Activity of the Suprarenal Gland in Health and Disease.—The thesis which is supported in this paper by CRAMER (*Report of Imperial Cancer Research*, 1919, vi, 1) is that the thyroid and adrenal gland functioning together form an apparatus for the heat regulation of the body by means of their internal secretions. A study of heat regulation or heat production is not undertaken, but the author centers his attention upon the morphological changes in the adrenal and thyroid. The observations were largely carried out on mice which were subjected to cold, infection, acidosis, hemorrhage and anesthesia. Experimental hyperpyrexia was associated with congestion and partial disappearance of the colloid of the thyroid. The author describes a method for the histochemical demonstration of adrenalin within the cells of the suprarenal. Osmic acid precipitates fine granules within the cells of the medulla, which may be differentiated from fat droplets. These are spoken of as adrenalin. Lethal doses of tetrahydronaphthylamine and severe exposure to cold act as powerful stimuli to the adrenal with massive secretion. The medullary cells

discharge their adrenalin (which may be seen in the veins) and then undergo lysis. This massive discharge causes congestion of the lungs and hemorrhage. Moderate stimulation of the gland leads to an increased output without an unloading of the adrenalin contained in the medullary cells. Thus the condition of the adrenal in relation to its secretion is dependent upon the intensity of the stimulus. Somewhat similar results were obtained by infection. With a streptococcus of low virulency the suprarenal was found to be in a state of stimulation without depletion of its adrenalin, while more virulent strains and infection by the organisms of gas gangrene led to marked exhaustion of the gland both of its adrenalin content of the medulla and the lipoids of the cortex. The author found that the lipoids of the cortex played a part with the medulla in the formation of adrenalin. Following postoperative shock the suprarenal was not exhausted but its tissues were still loaded with adrenalin granules and were actively secreting these into the central vein at a time when there was low blood-pressure and a subnormal temperature. This finding is claimed to be in agreement with that of Stewart who showed that there was no alteration in the quantity of adrenalin in shock from that of a normal animal. The entire work of Cramer is based upon the morphological demonstration of the functional activity of the thyroid and adrenal. Many points will require the biological test.

The Cultivation of Recently Isolated and Laboratory Strains of Human Tubercle Bacilli on Artificial Media.—CORPER (*Am. Rev. Tbc.*, 1919, iii, 461) used for cultivation sixteen different media having a basic composition of salt, ammonium phosphate and agar. He grew human tubercle bacilli which had been artificially cultivated for about one year on this basic agar with the addition of glycerol and one of the following: defibrinated rabbit's blood, egg, ground up tissue, beef extract and peptone. Old laboratory strains six to eight years old did not grow on this basic agar with glycerol alone. Recently isolated human tubercle bacilli revealed a disposition of growing only upon a few media. They grew most constantly on the glycerol agar with the addition of egg or rabbit's blood. A few of the strains grew on all of the media on which the old cultures grew. Some of the delicate strains would not grow even when egg or rabbit's blood was added. With both the recently isolated and the old cultures there was a distinct difference in the growth ability of the different strains.

An Investigation of the Acid Fastness of Tubercle Bacilli.—EHRLICH, KLEIN and MARMOREK observed that young tubercle bacilli are not acid-fast. Marmorek suggested that this was due to their not having had time to develop the fatty waxy capsule which is supposed to be responsible for the resistance to decolorization. Wherry modified this acid fastness by growing the organism on media unsuitable for the synthesis of fats and the development of the capsule. SUYENAGA (*Am. Rev. Tbc.*, 1919, iii, 473) was unable to corroborate the observations of Ehrlich, Klein and Marmorek. He transplanted a saphrophytic strain of tubercle bacilli every two days from the transparent edge where the growth is younger. The medium used was glycerol agar 0.8 acid to phenolphthalein. This rapid transfer for 334 generations had little effect on

the acid fastness of the organism. Growth upon the non-nutrient and the "ameba media" used by Wherry in his work, considerably reduced the acid fastness but did not altogether destroy it. He also found that reactions of culture media, varying from 1.5 acidity to 2.0 per cent. alkalinity to phenolphthalein had little effect upon the acid fastness of the tubercle bacilli.

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AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

The Prevention of Fatigue in Manufacturing Industries.—SPAETH (*Jour. of Industrial Hygiene*, 1920, vol. i, No. 9) states that the absence of a critical preliminary analysis has led to a confusion in the minds of certain physiologists between normal fatigue in industry ("industrial fatigue"), which is harmless, and cumulative fatigue, which is dangerous and may be associated with serious nervous disorders (industrial psychoneuroses). So far as we are aware there exists at present no valid quantitative physiological test for cumulative fatigue. Since normal fatigue may merge insensibly into cumulative fatigue, the reduction of normal fatigue to a minimum is the first logical step in a prophylactic attack. Normal fatigue may be reduced by a careful adaptation of all environmental factors such as illumination, ventilation, humidity, temperature, disposition of machinery, seating facilities, periods of rest, adequate and nutritious food, etc., to the physiological requirements of the workers. There is a great need for physical, physiological and psychological standardization of industrial workers by trades and processes. We have suggested a number of simple tests or types of tests that could be applied in a large variety of industries. Such tests are important for adolescents from fourteen to twenty years of age, as well as for men and women in industry. A number of physiological shortcomings of scientific management are discussed, especially the untrained type of time-study man and certain highly unscientific aspects of time and motion study methods.

Syphilis in Railroad Employees.—STOKES and BREHMER (*Jour. of Industrial Hygiene*, 1920, vol. i, No. 9) state that a general medical examination of 1763 patients of the Mayo Clinic showed 3.1 per cent. of them to have syphilitic infections obvious enough to be detected without the use of the routine Wassermann test. Four and two-tenths per cent. of the men and 2.6 per cent. of the women have

the disease. The lowness of these figures reflects, to some extent, the weakness of clinical judgment in the recognition of this disease as compared with current figures based on the routine Wassermann test. Part of the lowness of these figures is attributable to the large farming element in the clientele of the clinic and to the low incidence of venereal diseases in the States from which most of the patients are drawn. Of the railroad employees examined, 11.7 per cent. had syphilis. The disease was eight times as frequent in them as in farmers (1.5 per cent.), three times as frequent in them as in business men (3.8 per cent.), and twice as frequent as in laborers (6.1 per cent.). The doubtful value of the history of infection and the blood Wassermann test in the recognition of these cases is shown by the fact that 24 per cent. of the patients gave no history of infection other than gonorrhea; 62.5 per cent. had observed no secondary manifestations and 53 per cent. were completely Wassermann-negative on the blood. On the other hand, 64 per cent. of those whose spinal fluids were examined showed positive findings. Of the diagnoses, 58.7 per cent. were contributed by laboratory procedures; 41.3 per cent. were identified by routine physical examination. Of the men examined, 79.5 per cent. had syphilis of the nervous system; 18.7 per cent. had cardiovascular syphilis. Pupillary abnormalities, muscular paralyses and fundus changes were present in 62.5 per cent. of the cases. Of the cases examined, 65.1 per cent. showed abnormal knee reflexes, and similarly high percentages prevailed for the other simpler details of the neurologic examination. Definite mental symptoms were present in 38.4 per cent. The above findings suggest that the routine railroad medical examination is insufficient to protect the public from the dangers of syphilis in men concerned in the operation of trains. Three suggestions are made with a view to increasing the efficiency of the railroad medical examination with respect to the recognition of syphilis: (1) Routine Wassermann tests should be performed on all employees between the ages of seventeen and twenty-five years, by a competent State board of health laboratory, and repeated on all employees reaching thirty-two years of age. (2) There should be annual effective examination of men between the ages of twenty-five and forty rather than of men over fifty years. Such examinations should include more attention to pupillary reactions than is at present given, and should employ those fundamentals of the neurologic examinations, such as tests of the deep reflexes, Romberg, etc. These can readily be performed by competent general examiners. (3) Formal educational propaganda should be undertaken by railroad medical departments for the education of medical examiners and employees alike to the great significance of syphilis in industrial insufficiency and personal ill-health.

The Prevention of Simple Goitre in Man.—KIMBALL, ROGOFF and MARINE (*Jour. Am. Med. Assn.*, 1919, lxxiii, 1873) report results on the prevention of goitre based on the examination of girls in the public schools of Akron, Ohio, in grades from the fifth to the twelfth, inclusive, made from November 26 to December 3, 1918—nineteen months after beginning the prophylactic use of iodin. The method used was to administer 2 grams sodium iodide in 0.2-gram doses for ten consecutive school days, repeated each autumn and

spring. The results showed that simple goitre may be prevented on a large scale and that the method is practical and economical and can be recommended as a public health measure in goitre districts. The danger of iodism or of exophthalmic goitre from such amounts of iodin as were given is shown to be negligible.

Complement Fixation in Diagnosis of Tuberculosis.—MOURSUND (*Jour. Infect. Dis.*, 1920, xxvi, 85) states that the complement-fixation test for tuberculosis as described in his article is of no value as a diagnostic or prognostic aid. The complement-fixation test for tuberculosis with alcoholic extract of tubercle bacilli as antigen, is not specific. Not all complement-fixation tests with bacterial antigens are specific. A large percentage of serums giving a positive Wassermann give fixation with tubercle and gonococcus antigens. A certain number of individuals not infected with tuberculosis or gonorrhea will give positive fixation tests with one or both of the corresponding antigens.

The Fate of Bacteria Introduced into the Upper Air Passages.—BLOOMFIELD (*Am. Rev. Tuberculosis*, 1919, iii, 553) states that the general result of his experiments indicates that even after a short period of time it is usually impossible to recover sarcina lutea swabbed in large amounts on the tongue, nasal mucosa, or into the crypts of the tonsils. Whereas, disappearance from the nose was somewhat slower than from the other sites, in only one case could any organisms be recovered after twenty-four hours, and in none after two days. Cultures made in this way do not, of course, prove the complete absence of the microörganism in the mouth and nose, but the general trend of the quantitative relations indicates a rapid disappearance. The fact that the estimated dose of 50 to 100 billion organisms was vastly greater than that in any natural infection, indicates the remarkable efficiency of the mechanism present in the upper air passages for disposing of this organism. An analysis of the possible factors active in effecting this disposal indicated that recation of mouth secretions, mechanical action and other mouth bacteria play little, if any part, but the saliva and mouth secretions exert a prompt and marked bactericidal effect. Similar methods are being used in studying the fate of other microörganisms introduced into the upper air passages.

Potency of Antimeningococcic and Antipneumococcic Serums.—The measure of control enforced at the Hygienic Laboratory of the U. S. Public Health Service (*Public Health Reports*, 1919, xxxiv, 2657) with respect to the serums used in the treatment of pneumonia and meningitis are described in great detail. In each case it is required that the serum under test shall compare favorably with the standard. In the case of the antipneumococcus serum a mouse-protection test is employed, while serological methods are depended on for evaluating the antimeningococcus serum.

Closing Schools as a Means of Controlling Epidemics.—Committees of the United States Bureau of Education and of the American Public Health Association (*Public Health Reports*, 1919, xxxiv, 2668)

as the result of an investigation report that the successful control of epidemic disease among school children requires: (1) Keeping the schools open, with the possible exception of sparsely-settled rural districts when medical inspection cannot be obtained and where aggregation takes place only in the schools. (2) Careful daily or frequent periodical inspection of schools. (3) Careful provision for exclusion of cases and contacts, emphasis being placed on clinical data rather than upon fixed periods of exclusion. (4) Systematic home visitation. (5) Reliance upon natural and physical cleansing rather than upon chemical disinfectants.

Steam as a Bedbug Eradicator.—The Public Health Service (*Public Health Reports*, 1919, xxxiv, 2713) describes the destruction of bedbugs in a large bunk-house in which it was possible to subject the whole interior of the building to steam. A temperature of 160° F. maintained for three hours was found to be effective. The building was still free from bugs two months after the steaming.

Botulism from Eating Canned Ripe Olives.—ARMSTRONG and STORY (*Public Health Reports*, 1919, xxxiv, 2877) report an outbreak of 14 cases of botulism from the eating of ripe olives. Seven of the cases proved fatal. The circumstances of the outbreak were such as to render study by epidemiological methods very easy. Such methods point directly to the olives as the source of the poisoning, and an examination of some of the suspected material showed it to contain the toxin of the *Bacillus botulinus*. The olives in question were remarked to be of abnormal taste, and closer examination showed that they were certainly spoiled. Only three persons among the seventeen who ate of the spoiled olives failed to develop clear indications of botulism. Under the section on prevention the author states that: (1) The epidemiological investigation points to the ripe olives as the vehicle of the poison. (2) The olives and brine were found to be highly toxic for animals, both when fed and when injected. (3) The organism isolated from the olives and brine seems, from its morphology, cultural characteristics, toxin formation, and from the symptoms and pathological lesions produced, to be a strain of *Bacillus botulinus*. (4) Antitoxin and agglutinins could not be demonstrated in the blood of recovering patients forty-five days after the dinner. (5) Alcohol has the property of neutralizing the toxin when mixed *in vitro*. (6) It would seem that *Bacillus botulinus* does not produce its toxin under usual conditions in a warm-blooded animal.

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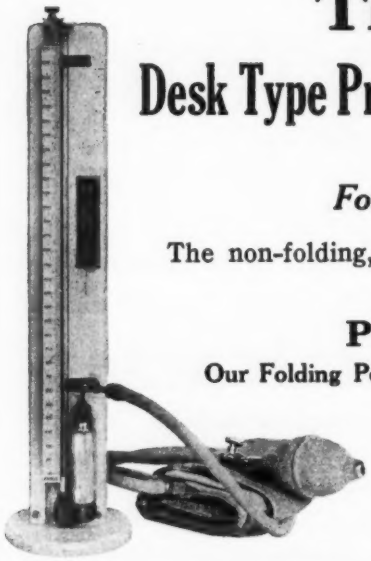

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Physicians are requested to send for literature detailing treatments, Mineral Springs analyses and other particulars.